Semi-Annual Report

(Spring 1966)

Project Summary - 1966

Interdisciplinary Space Science Grant

NASA - NsG-298

Investigator	Dept.	Title	Amount Requested	Amount Authorized
Moore	Elec. Engr.	Scattering of Waves	$ 4300	$ 4300
Talley	Elec. Engr.	Semi-conductor Surfaces	10000	10000
Daugherty	Elec. Engr.	Wide Band Frequency Multiplier	11100	11100
Adams	Chemistry	Biochemical Energy Conversion	22000	10000
Dusanic	Microbiology	Effects of Ionizing Radiation	9923	6000
Willems	Civ. Engr.	Dynamic Stability of Stiffened Plates	7750	3800
Elbel	Phys. Educ.	Telemetering Pulse Rates of Men During Exercise	1750	1750
Lal	Pharmacy	Behavioral Effects of Drugs under Limited Sensory Stimulation	3100	3100
Leaders-Norton	Pharmacology	Cardiovascular Response under "Zero-g" conditions simulated by reducing sensory input	6000	5000
Barr-Gatts-Saunders	M.E.-Business	Technology Utilization - Information Retrieval	3300	2800
Warfield	Elec. Engr.	High Speed Random Bit Source with Equal Transition Probabilities	3200	3200
Kaesler	Geology	Evaluation of Methods of Numerical Taxonomy in Palientology Using Selected Species of Fusulinarea	7650	7650
Willems	Civil Eng.	Analysis of Plates of Variable Thickness	1000	1000
Kohlman	Aerospace Eng.	Engineering Development of the Parafoil	1500	1500
Talley-Prosser	Elec. Engr. & Physics	Lithium-Drifted Semiconductor Junctions; Their Dependence on Semiconductor Material Properties and their use as Nuclear Particle Detection	14650	14650
Leone-Baxter	Zoology	Thermal Denaturation Profiles of DNA from a Variety of Animals	2000	2000
Himes	Comp. Biochem	Complete Biochemistry of a Thermophile	4000	4000

#2

Lenzen	Engr. Mech.	Vibrations in Isotropic Hollow Torus	$ 2500	$ 2150
Fitch-Shirer	Zoology	Natural Environmental Factor in Behavior of the Opposum, Racoon, and Striped Skunk	1400	1400
		Project Total	$117923	$95400
		Honorarium, Seminars, Travel to Space Centers, etc.		4600
		Total Authorized 1966		$100000

CRES CENTER FOR RESEARCH IN ENGINEERING SCIENCE
THE UNIVERSITY OF KANSAS · LAWRENCE · KANSAS

February 25, 1965

Memorandum to: K. U. NASA Committee

From: R. K. Moore

Subject: Request for Extension: Theoretical Study of Scattering of Waves From a Rough Surface.

For the past two years, various efforts in theoretical scatter study have been conducted under CRES Project 30C and 40N. As our other related research has grown, the need for support for theoretical studies associated with radar return from the moon has continued. Our NASA projects on which we are currently working are aimed at experimentation and at interpretation of images. The theoretical work on lunar scatter does not fall in these categories, nor is it appropriate for our National Science Foundation grant which is concerned with more general scatter problems than the back-scatter from the moon.

The contemplated work represents a continuation of that done previously. Previous work has resulted in a number of papers (see List of References).

Since it may be necessary to perform some experimental checks in the acoustic simulator, the budget includes a small item for supplies. The principal medium of publication for the work on this project has been the Journal of Geophysical Research which has a significant page charge. Accordingly, an item is included in the budget to include the page charges.

BUDGET:

Instructor (half time, 12 months)	$3,600
Supplies	200
Publication Charges	500
TOTAL	$4,300

According to latest reports, Project 40N is about out of funds. Accordingly, early action on this request would be greatly appreciated.

RKM:ks

LIST OF REFERENCES

Fung, A.K. "Theory of Radar Scatter from Rough Surfaces Bistatic and Monostatic, with Application to Lunar Radar Return," J. Geophys. Res. 69, No. 6, pp. 1063-1073, March 1964.

Fung, A.K., and R.K. Moore. "Effects of Structure Size on Moon and Earth Radar Returns at Various Angles," J. Geophys. Res. 69, No. 6, pp. 1075-1081, March 1964.

Fung, A.K., R.K. Moore, and B.E. Parkins. "Notes on Backscattering and Depolarization by Gently Undulating Surfaces," J. Geophys. Res., March 1965.

A Request
to
The University of Kansas
Committee on Space Science and Technology

for

Funds to Support an Investigation

on

THE STUDY OF SEMICONDUCTOR SURFACES USING METAL-OXIDE-SEMICONDUCTOR STRUCTURES

Submitted By

H. E. Talley

Electrical Engineering Dept.

February 25, 1965

Proposal for the Study of Semiconductor Surfaces Using Metal-Oxide-Semiconductor Structures

It has long been realized that the fundamental limitation of the operating life of semiconductor devices appears to be the designer's ability to control the properties of the semiconductor surface. A very large percentage of the device designer's efforts have been directed toward improving the reliability (aging performance) of his devices. These efforts have gone in several directions: carefully designed metallurgical and chemical fabrication procedures, development of means to partially isolate the surface from the ambient through a semi-permeable intervening layer, much improved control of the ambient in which the device exists, etc. As a result of this work there have been rather remarkable increases in transistor operating life, but as performance capabilities increased so did systems demands, so that more and more stable devices have been required, particularly in missile and computer applications. Thus it has more than ever become important to understand the fundamental nature of the processes which occur at semiconductor surfaces.

In spite of the amount of work expended in studying the reliability of devices and the performance improvements which have been achieved, the semiconductor industry has accumulated remarkably little knowledge of a fundamental nature applicable to semiconductor device surfaces. The reason for this is twofold. As a commercial industry their prime concern is immediate and

practical results. Understanding problems often seems less important than being able to solve them. This pragmatic approach tends to work at cross purposes with basic studies. Secondly, the device parameters available for measurement involve such complicated inter-relationships, that it is virtually impossible to isolate the surface dependent factors from the myriad of other factors resulting from the fabrication procedures. Thus a great deal is known about how to make reliable transistors, but surprisingly little is known as to why they are reliable.

Recently, however, a new measurement technique has become available which promises to provide information previously virtually inaccessible. This technique involves the use of the metal-oxide-semiconductor (MOS) diode. In principle the construction and use of this device is very simple. For example, using silicon as the semiconductor material an oxide is deposited on the surface. This oxide might be thermally grown or chemically deposited. A metal dot is then evaporated on the oxide. Electrical connections are made to the bulk semiconductor and the metal dot and the capacitance-voltage curve for the three element system (metal-oxide-semiconductor) is measured. From this C-V curve can be inferred the density and location of the energy states within the forbidden energy region at the semiconductor surface.

Basically the surface characteristics of a material are describable in terms of the surface potential, and this can be inferred from the energy state distribution at the surface and hence from the MOS C-V curve. One would suspect, therefore, that measurements of this sort made using surfaces prepared exactly

as in device fabrication could be very fruitful. Preliminary results show this to be the case.

A large number of experiments come to mind which could be important. Without going into great detail, three particularly signigicant ones can be cited:

a) The growth of a thermal oxide on silicon invariably leads to the surface tending toward n-type. This has made and continues to make pnp silicon transistors unstable and difficult to fabricate. The reason for this effect is not known; it is most important that an explanation be found.

b) There is an unexplained interaction of the metallic contact with the semiconductor surface in an MOS diode. The oxide is generally so thick and the times involved so short that metal ion migration seems highly unlikely, and yet there are quite reproducible results showing that some metals are much more "reactive" than others. This, too is of substantial interest to the semiconductor industry where the role of contact metals has long plagued the aging performance of devices.

c) While the nature of the energy states arising in the bulk material from impurities is well-known, there has been no attempt to deduce the nature of these same energy states at the surface. There is reason to suspect that they may play an important part in the surface properties of the semiconductor material.

These three experiments by no means exhaust the obvious things which should be tried. These do seem, however, particularly important. Further, each of these experiments---and especially the first and second---potentially are quite important to the semiconductor device industry.

The purpose of this proposal is to request funds to allow initiation of a program to study MOS structures as vehicles for investigating the surface properties of semiconductor materials and devices. Attached is a proposed budget for this project.

The items listed under Salary are rather self-explanatory. The graduate research assistant would be hired for an eleven month period beginning in September of this year. The student assistance would be that of an undergraduate, and would be for the two semesters of the 1965 academic year. The half-time salary for me would be to cover the summer months of this year.

The list of equipment as shown is not adequate to carry out the experiments described above. There are, however, two possibilities being explored which could make it adequate. First, negotations are underway with Bell Telephone Laboratories to obtain diffusion and oxidation equipment as part of their college gift program. The prospects for obtaining it appear bright but not certain. Second, as part of the NSF undergraduate laboratory program, equipment has been requested to allow the establishment of undergraduate physical electronics and semiconductor laboratory courses. Certain of the items which were requested will be needed in the MOS studies, but without japardizing their effectiveness as laboratory facilities. It is probable that the MOS

program could be started without the Bell Laboratories gifts, but the work would be very difficult to undertake without several of the NSF items. Unfortunately approval of the NSF proposal cannot be obtained proir to May 1, 1965. The probability of receiving the NSF grant is sufficiently large, however, to ask that the proposal being submitted here be approved.

Proposed Budget

(Period: June 1, 1965-June 1, 1966)

1. Salaries

Graduate research assistant	$2100.	
Undergraduate student	500.	
H. E. Talley ($\frac{1}{2}$ time, 2 months, Summer 1965)	1389.	
Total		$3989.

2. Equipment

a. Diffusion tubes		
Quartz	500.	
Mullite	350.	
b. Moisture Monitor	600.	
c. Gas driers	1950.	
d. Flowmeters	300.	
e. Oven	150.	
f. Controlled atmosphere enclosures	525.	
g. Photo-resist developing table	75.	
h. Hot plates	120.	
i. Silicon material	400.	
j. Inspection Microscope	450.	
k. Glassware (Quartz diffusion glassware, push rods, diffusion trays, quartz breakers)	285.	
l. Chemical (Phosphorus and boron diffusion sources, deposited oxide sources, solvents, etchants)	175.	
m. Miscellaneous materials (lapping and polishing compounds, angle lapping blocks, scribing tools, evaporation filaments, etc.)	220.	
Total		$6100.

Total $10089.

ELECTRICAL ENGINEERING DEPARTMENT
SCHOOL OF ENGINEERING AND ARCHITECTURE
THE UNIVERSITY OF KANSAS
LAWRENCE, KANSAS

March 15, 1965

KU Committee on Space Science and Technology
School of Engineering and Architecture
University of Kansas

Gentlemen:

Attached is a request to the University of Kansas Committee on Space Science and Technology for support of an investigation in the area of precision measurement in electrical engineering.

It is felt that the results of the work that is proposed can be of significant industrial importance. The research relates directly to the quartz crystal industry but is not limited in application.

Thank you for your consideration.

Sincerely,

Don L. Daugherty

D. G. Daugherty
Assistant Professor
Electrical Engineering

Approved:

W. P. Smith
Chairman
Electrical Engineering

Proposal for the Development of a Wide Band Frequency Multiplier

Modern methods for measuring the frequency of an AC electrical signal are highly refined. The most widely used measurement system is a digital counter. The digital method consists of counting the number of cycles of the unknown signal occurring in a well defined period of time. If the time is chosen as, say, one second, the counter conveniently reads directly in cycles per second. Instruments of this type are manufactured by many companies and are in general use. The most salient features of the method are the wide band width of the counters and the convenient visual readout. If, however, one wishes to make frequency measurements such that the result reads in tenths or hundredths of cycles per second, the measurement time must be increased to ten and 100 seconds. Increasing accuracy thus corresponds to increased measurement times. Such a requirement is quite common and the digital counter user faces a problem that seems without adequate solution. The problem is that increased measurement times are either impossible or too costly and inconvenient. Picture, for example, a production situation that requires 100 or 1000 seconds of waiting time for each measurement. The solution is not a happy one. A frequency multiplier can be constructed such that the unknown signal is multiplied by a suitable integer (10, 100 or 1,000). When this is properly done, the measurement time is decreased without loss of accuracy. The price that is paid for this decreased time is loss of bandwidth. The frequency is now measurable over only about a one percent bandwidth and this is generally intolerable. Quartz crystal manufacturers, for instance, produce crystals in a wide range of frequencies and the notion of keeping dozens of multiplier devices to cover all possible frequency bands is impractical. Nevertheless, the choice of method is clearcut and one must decide on the lesser of the evils in order to obtain the accuracy required in the time allowed.

It is possible in some cases to measure the period of a waveform by using a digital counter. The measurement results are not read directly as frequency but the method is useful mainly at very low frequencies. The proper solution to the entire problem is to develop a practical method for multiplying frequency in a wideband frequency multiplier, so that direct cycle counting in short measurement times can be employed.

Recently a method for multiplying a wide band of frequencies in the audio range (300 - 3,000 cps) has been demonstrated. The method employs a novel arrangement of communications circuits so connected that the unknown low frequency is translated to a much higher frequency, multiplied, and returned to the audio range. The method works well at audio frequencies and is apparently adaptable to the frequency range of 10 kcs to 1 mcps. Although the audio range is of interest, a multiplier with an input bandwidth of a megacycle in the low radio frequencies would be of much importance in the quartz crystal industry. Manufacturers of quartz resonators are pressed for high precision frequency measurements in the face of high volume production. Thus, time wasted in measurements adversely affects unit costs.

The feasibility of this has yet to be demonstrated and further, the detailed analysis of the output signal of the present wideband audio multiplier is incomplete.

It is the express purpose of this research to a) provide a rigorous analysis of the recently developed wideband frequency multiplier system and b) demonstrate the usefulness of the system over a very wide frequency range. It is proposed that a working model of a frequency multiplier with a three decade input bandwidth (1 kcps to 1 mcps) be designed, constructed and tested.

The proposed experimental work will require some special electronic test equipment as well as some specialized supplies and will be carried out during the nine-month period beginning in late June, 1965. The schedule of the requested funds is as follows:

Equipment:	
500 mc frequency counter	$ 3,000
Tektronix oscilliscope	1,550
Spectrum analyzer plug in units	2,900
R. F. millivoltmeter	750
Materials and supplies	1,250
Salary:	
Graduate student (2 months)	554
TOTAL	$10,004

add 4 months
1/3 time
1108
$ 11,112

Submitted by:

D. G. Daugherty
Assistant Professor
Electrical Engineering

Approve to $16,000 max
no comp. - but OK not more than ½ PD [illegible]

Title of Proposal:

FUNDAMENTAL STUDIES OF BIOCHEMICAL ENERGY CONVERSION SYSTEMS

Principal Investigator:

Ralph N. Adams, Department of Chemistry, University of Kansas

Interest in bioelectrochemical energy conversion systems has become of increased importance especially in closed ecological systems for space operations. The first symposium on biochemical fuel cells (BFC's) reveals the general scope of the work[1]. BFC's may be indirect, in which an enzyme or other biochemical reagent generates a suitable electrochemically active intermediate for electron transfer. The direct BCF may employ enzyme-substrate complexes interacting directly with electrode surfaces. The entire area of biochemical energy conversion also includes solar energy conversion systems.

In biological oxidation-reduction processes of the type which can conceivably provide continuous or semi-continuous energy conversion, one is concerned with a substrate molecule, A, which undergoes a series of complex oxidation-reductions, followed by various chemical reactions with other components of the system, C, as:

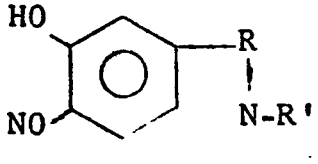
$A \pm ne \rightarrow B$	electron transfer
$B + C, etc \rightarrow D$	chemical reactions
$D \pm ne \rightarrow Product$	electron transfer

The continuous series of electron transfer steps with concurrent chemical reactions provide electroactive species for the energy removal in the form of available electrons.

Two main problems exist in the practical realization of such an energy conversion system. First, the manner in which the electrons can be abstracted from the working anode constitutes a problem of major technological concern. Here ingenuity in the design of catalytic electrode surfaces, low resistance networks, etc, are of prime importance. However, of even more importance, is an understanding of the basic electrochemistry of A, B, D, etc. The following example is illustrative of the complexity.

The catacholamines are a series of extremely important biological molecules widely distributed in mammalian metabolism processes. Although they do not constitute a substrate particularly important to BFC's, they illustrate the complexity of the organic electrochemistry which prevails in such systems.

The catacholamines can be represented by the generalized structure A:

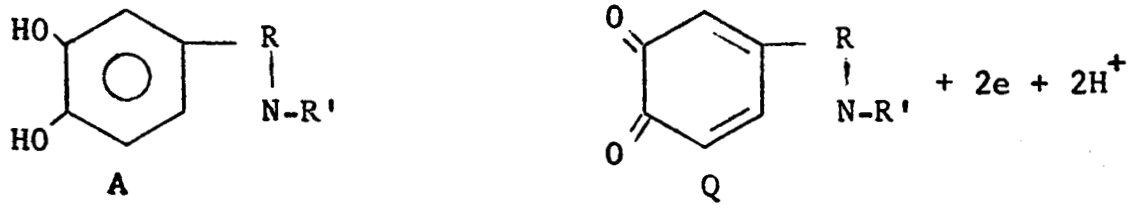


A

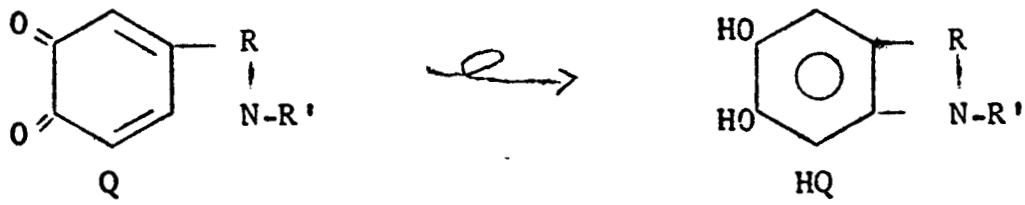
(the side chain skeleton is simplified for this illustration. With various substituents, these molecules are commonly known

as adrenalin, nor-adrenalin, dopamine, etc. They will be recognized as important intermediates in brain activity, smooth muscle action, etc.).

The typical catacholamine is electroactive and loses two electrons upon oxidation, to give the corresponding quinone:



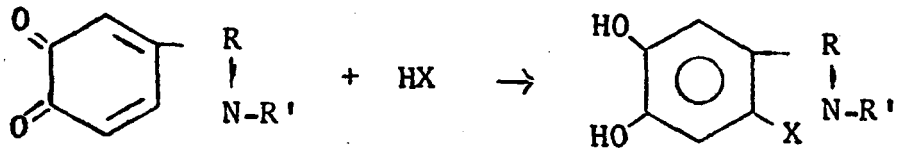
The quinone, Q, is a highly reactive ortho-quinone which undergoes so-called 1,4 additions. One of the simplest of such addition reactions is the internal oxidation-reduction cyclization:



The resulting cyclic hydroquinone, HQ, is now more easily oxidized than the starting A and so the chain of redox sequences goes on.

However, if this reaction is carried out in the presence of other 1,4 addition agents, Z, which can be as simple as dilute

mineral acids, than the following reactions can interfere with the cyclization:



Now, an entirely new series of redox steps may develop. By such a simple alteration in the medium in which the reaction takes place, entirely new substrate systems are produced. The relative rates of the competing steps determine the over-all course of the reaction.

The above redox reactions for the catacholamines definitely exist <u>in vitro</u> and there is a longstanding argument in the biochemical literature over their existance <u>in vivo</u>. It must be noted that other enzymatic reactions add greater complexity to the above system <u>in vivo</u>. The rates of the various cyclizations and competing reaction have only been measured within the last months in the senior investigator's laboratory.

The point of the above illustration is that such organic electrochemical reactions are the very basis of biological energy conversion systems. The electrochemistry of these systems is simply not known. More important, the electron transfer mechanism of even simpler aromatic and heterocyclic substrates have not yet been studied. A survey of the open literature of

electrochemical energy conversion reveals no serious attention has been given to this aspect of the work.[1-3]

Specifically, we wish to investigate the oxidation-reduction mechanisms of selected aromatic and heterocyclic substrates as model (and potentially practical) systems for biological energy conversion systems. These will predominately be aromatic amino and hydroxy compounds since they constitute a large proportion of biologically reactive systems. Specific systems selected for their relevance to mammalian and microbiological redox processes will be examined with regard to their overall oxidation-reduction pathways at solid electrodes (only the latter are of conceivable interest in BFC's). The techniques applied will be those found to be very successful in our past approach to organic electrochemistry. These include cyclic voltammetry, constant current programs, and high-speed coulometry. In addition, electron paramagnetic resonance (EPR) methods are to be used to identify free radical intermediates and fast solution spectrophotometry will be used where applicable.

All of the equipment necessary for such investigations is available in the senior investigator's laboratory. Only one piece of permanent equipment is requested in the budget. This is a visual read-out analog simulator to examine the complex electrochemical and EPR wave forms which are encountered in

these systems. It must be admitted the work can be carried out in most cases in the absence of this device. However, the potentialities of this device indicate that far more information may be forthcoming on even the simpler systems with its use and it will be indispensable for some of the redox systems to be studied.

It is believed that the background experience gained over the past years will enable us to effectively begin the studies outlined herein. A list of recent publications from the senior investigator's laboratory particularly pertinent to this area is attached.

References Cited

1. Biochemical Fuel Cells, symposium in "Developments in Industrial Microbiology", Vol. 4, Pridemark Press, Baltimore, 1963.

2. Sisler, F. D., Missiles and Rockets, April 17, 1961.

3. Allen, M. J., Electrochim. Acta., 7, 931 (1964).

BUDGET: (1 Year)

SALARIES	
One (1) post-doctoral research associate, full time, 12 months *	$6,500.
Two (2) graduate assistants, 1/2 time, 12 months @ $222./month	5,332.
One (1) research technician, 1/2 time, 12 months	2,000.
EXPENDABLE SUPPLIES	
Purified solvents, expendable glassware, electronic maintenance	2,000.
PERMANENT EQUIPMENT	
One (1) analog simulator, operational amplifier type with visual display, for complex line shape evaluations	7,000.
(The proposed price of this instrument is between $7-8,000., a firm price is not yet available.)	
Total	$22,832.

If granted, this project could begin immediately. A suggested starting date would be 1 June 1965.

* A post doctoral candidate already trained in this area is available to work on this project.

EFFECTS OF IONIZING RADIATION ON RESISTANCE TO A METAZOAN PARASITE

A research proposal submitted to the University Committee on Space Science and Technology

University of Kansas
March 31, 1965

Donald G. Dusanic
Assistant Professor of Microbiology

and

M. J. Freeman
Assistant Professor of Microbiology

Introduction: Man may encounter a variety of radiations in space. The harmful effects of these radiations on organisms have been recognized and studied extensively (Behrens, 1959). Such investigations considered the physiological, pathological, and immunological alterations caused by radiations (Taliaferro et al., 1964). Elucidation of the effects of radiations on the ability to resist infections has received considerably less attention.

Studies utilizing relatively simple antigens to examine the effects of radiations on serological responses have shown that radiation may significantly alter the production of antibodies. The usual effect observed has been a depression or delay of antibody production, although less frequently, depending on the time of exposure to radiations with respect to immnization, enhancement of antibody production has been demonstrated (Taliaferro and Taliaferro, 1964).

Investigations of the effects of radiations on the responses of animals to infectious agents have been concerned primarily with bacteria and protozoa. Relatively little has been done in the area of immunity to metazoan agents. Among the metazoa are numerous important human parasites, some of which are well suited for this type of study. Trichinella spiralis is one such parasite. The worm resides in both the intestine and the tissues. After the ingestion or oral administration, the larvae penetrate the mucosa and return to the lumen of the intestine, reaching sexual maturity by the second day. Doses for various experimental animals have been established. Copulation and fertilization occur, and larva are produced by the seventh day. These larvae penetrate the mucosa and migrate to the voluntary muscle. They are most numerous

in the blood from the eighth to the twenty-fifth day. Adults are short lived and are expelled from the intestine (Gould, 1945). Infection initiates a pronounced eosinophilia. The immunological response is marked (Kagan, 1960). Eleven antigens have been demonstrated in the larvae (Tanner and Gregory, 1961; Tanner, 1963a, 1963b). Ten of these are proteins destroyed by proteolytic enzymes. One of the antigens is not denatured by the enzymes. Four distinct antigens have been demonstrated in the adults. Excretion-secretion products have also been shown to contain antigens and stimulate antibody formation. A sequence in the time of appearance of antibodies to the larval antigens of both the somatic extracts and the secretion and excretion products has been observed in the rabbit (Dusanic, unpublished). This prior work, coupled with the varied antigens eliciting a variety of antibodies and the fact that a high degree of immunity is established after infection, make Trichinella spiralis an excellent organism for use in a study of radiation effects.

Gould et al. (1953) showed that 750,000 roentgens (r) of X-ray killed larvae in vitro, while doses of 5,000 to 6,000 r inhibited development of larvae into adults. 3,500 r gamma radiation caused sterility in female worms in vivo, while 18,000 r inhibited larval development (Gomberg and Gould, 1953).

Parasites are generally less radiosensitive than their hosts. Mice exposed to gamma rays were found to be more susceptible to Trichinella infection and there did not appear to be a significant alteration in the precipitin titers (Stoner and Hale, 1952). However, no attention was given to the period of exposure to radiation with respect to infection or to the temporal aspects of antibody formation such as difference in the times of appearance of specific antibodies. Larsh et al. (1962)

demonstrated changes in the histopathology of the intestine of immunized mice irradiated with 450 r of X-rays. They showed that the inflamatory response was smaller 8 days after irradiation and larger 12 days later than the non-irradiated controls suggesting that the immune response was significantly delayed.

The hazards of radiations encountered by astronauts in space may affect their ability to cope with infectious agents. This project proposes to study the effects of single and multiple doses of ionizing radiation on the susceptibility of animals (rabbits) to infection. The animals will be irradiated before, during and after exposure to Trichinella spiralis infective larvae. Various parameters will be considered in this investigation, such as the effects of irradiation on the cellular responses by periodic total and differential blood counts and the intensity of infection by larval counts from biopsied tissue. Following infection and irradiation several of the newer, sensitive immunochemical and physicochemical techniques will be applied to detect subtle variations in the host's response and resistance. By these methods alterations in the total resistance to infection (i.e. both innate and specific acquired resistance or immunity) will be evaluated. Serological and biochemical analyses will be performed in order to establish the temporal appearance of antibody to specific adult and larval somatic antigens and secretion-excretion antigens and to assay titers of antibodies to these antigens. The restoration of the normal state after irradiation will also be examined in terms of the above parameters and the effects of various restorative agents, such as colchicine, nucleic acids and kinins, will be evaluated (Jaroslow and Taliaferro, 1962).

Plan of procedure: Rabbits will be exposed to single and multiple doses of X-irradiation totaling 500 r (LD_{50} per 30 days is 700-825 r). In the preliminary experiments rabbits will receive single doses of 500 r X-irradiation 4 days prior to infection, immediately after infection, and 4 days after infection with 10 Trichinella spiralis larvae per gram body weight. Controls in these experiments will include normal rabbits, infected rabbits, and normal-irradiated rabbits. Total and differential blood counts will be performed daily before and after irradiation of the animals to evaluate the general physiologic effects of the irradiation and the effects of the infection on these processes. The effects of irradiation on production of larvae will be estimated by biopsy of the rabbit diaphragm, followed by digestion of the tissue with a pepsin-hydrochloric acid solution, and a count of the larvae per gram of tissue.

Rabbits will be bled at weekly intervals to collect sera for antibody assays. Adults and larvae will be incubated in saline solutions to collect secretion-excretion substances and homogenized and extracted with saline for somatic substances. Rabbit sera will be examined for antibodies by Ouchterlony precipitin tests, immunoelectrophoresis, and radioimmunoelectrophoresis (using isotopically labeled T. spiralis secretions and excretions and somatic extracts). These studies will characterize the antigen-antibody reactions and indicate alterations in the temporal appearance of the specific antibodies. Quantitation of these alterations will be accomplished by precipitin tests such as the P-80 test employing isotopically labeled parasite extracts and secretion-excretion products and by complement fixation tests.

Relatively large quantities of the Trichinella can be collected. Purification of the antigens may be performed by column chromatography,

electrophoresis, ultracentrifugation and other physical and biochemical procedures if suggested or warranted by the results of the above experiments. Biochemical analyses may be performed to characterize more specifically the reacting antigens and antibodies.

Additional studies will include multiple exposures to the x-irradiation before, before and after, and after infection. The resotration of the immune state and the effects of colchicine, nucleic acids and kinins on the acceleration of this process will be examined using the above techniques.

Significance: These experiments are designed to determine the effects on the host's resistance of irradiation before, during and after exposure to an infectious agent. Although the gross pathologic effects of irradiation are well known, the more subtle effects of irradiation upon the complex homeostatic mechanisms of the body are not as well understood. The effects of ionizing radiation over periods of time as might be encountered during exploration of outer space may be of considerable importance in the ability of man to cope with infection. The exact effects of irradiation upon resistance to infectious disease and the host-parasite relationship is difficult to predict accurately. Adverse effects of irradiation on resistance might be manifested either during or after space travel. The potential hazards from exacerbation of latent, subclinical infections of terrestrial origin as the result of irradiation would also appear to be of considerable significance to the health of space travelers. The latter factor may be of particular significance in view of the debilitating effects of unfavorable environmental influences and other stresses upon health. Extrapolation to man of the results from the proposed study may provide some insight into the basic effects of irradiation and perhaps suggest some means for the corrections of such effects through the use of restorative chemical agents.

References:

1. Behrens, C. F. 1959. Atomic Medicine, Ed. 3 Williams and Wilkins, Baltimore.

2. Dusanic, D. G. Unpublished observations of studies initiated in 1964 at University of Kansas.

3. Gomberg, H. J. and Gould, S. E. 1953. Effects of irradiation with cobalt-60 on Trichina larvae. Science, 118: 75

4. Gould, S. E. 1945. Trichinosis. Charles C. Thomas, Springfield.

5. Gould, S. E., Van Dyke, J. G. and Gomberg, H. J. 1953. Effect of X-rays on Trichina larvae. Am. J. Path., 29: 323.

6. Jaroslow, B. N. and Taliaferro, W. H. 1962. Restoration of hemolysin-forming capacity in irradiated rabbits and its relation to induction of antibody synthesis. The effects of ionizing radiations on immune processes. C. A. Leone, ed., Gordon and Breach, New York.

7. Kagan, I. G. 1960. Trichinosis: a review of biologic, serologic and immunologic aspects. J. Infect. Dis., 107: 65.

8. Larsh, J. E., Jr., Race, G. J. and Yarinsky, A. 1962. A histo-pathologic study in mice immunized against Trichinella spiralis and exposed to total body x-irradiation. Am. J. Trop. Med. Hyg., 11: 633.

9. Stoner, R. D. and Godwin, J. T. 1952. The effect of cobalt-60 gamma radiation on susceptibility and immunity of trichinosis. Proc. Soc. Exper. Biol. and Med., 80: 510.

10. Tanner, C. E. and Gregory, J. 1961. Immunochemical study of the antigens of Trichinella spiralis larvae. I. Identification and enumeration of antigens. Can. J. Microbiol., 7: 473.

11. Tanner, C. E. 1963. Immunochemical study of the antigens of Trichinella spiralis larvae. II. Some physicochemical properties of these antigens. Exper. Parasit., 14(3): 337.

12. Tanner, C. E. 1963. Immunochemical study of the antigens of Trichinella spiralis larvae. III. Enzymatic degradation of the major precipitating antigen. Exper. Parasit., 14(3): 346.

13. Taliaferro, W. H. and Taliaferro, L. G. 1964. The relation of radiation dosage to enhancement, depression, and recovery of the initial Forssman hemolysin in rabbits. J. Infect. Dis. 114: 285.

14. Taliaferro, W. H., Taliaferro, L. G. and Jaroslow, B. N. 1964. Radiation and Immune Mechanisms. Academic Press, New York and London.

Annual Budget, Initial Year:

A. Personnel	
1) Research Assistant, full-time, 12 months	$4,600
FICA and Retirement	350
2) Principal investigators, 2 months, one-half time (summer)	
D. G. Dusanic	833
M. J. Freeman	1,000
B. Supplies	
1) Laboratory glassware, pipettes, routine reagents, enzymes, kinins, colchicine, nucleic acids and special reagents	1,500
2) Radioisotopes (I^{131}, I^{125}, S^{35})	500
C. Experimental animals and maintenance	800
D. Minor special equipment	
1) Imhoff settling cones	90
2) Tissue grinders	100
3) Waring blendor, heavy duty	150
E. Total amount requested, initial year	$9,923

Period of support requested subsequent years: Support is requested for two additional years. It is anticipated that the increased scope of the work and increased costs will necessitate an annual budget of the same size as that of the initial year.

To: Committee for NASA Research Proposal

From: Nicolaas Willems

Date: July 15, 1965

Title: "Investigation of Dynamic Stability of Stiffened Plates Subjected to Pulsating Loading"

Objectives and General Significance: To determine theoretically as well as experimentally the dynamic stability of single skin stiffened plates subjected to periodic in-plane boundary loading. The theoretical analysis will be concerned with the onset of dynamic instability. Boundary conditions will be considered which are practical and can be realized experimentally. The periodic loading can be of the sinusoidal, square wave, or triangular type and pending on the theoretical implications and the experimental limitations one or more of these types will be considered.

This topic is of importance when dealing with stiffened plates as occur in aircraft, space structures, etc.

This study will serve as research material for the doctoral dissertation of Mr. R.C. Duffield (MAE).

Results to date: A certain amount of research has been done in the area of rods and columns under pulsating loads 1, 2, 3, 4 . Also some experimental results are available for these one dimensional structures 5, 6, 7 . In the area of plates almost all work to date has been for isotropic unstiffened plates under sinusoidal loads 1, 8, 9, 10 . S.A. Ambartsumyan and A.A. Khachatryan 11 have investigated the dynamic stability of an orthotropic plate (under certain conditions a stiffened plate may be treated as an orthotropic plate). Their investigation was limited to simply-supported boundary conditions and sinusoidal longitudinal loads. No experimental data are available. Considerable work has been done in the field of shells 1, 12, 13 with some experimental verification for very special cases 14, 15 .

Plan of Procedure:

1. To develop the theoretical analysis of single skin stiffened plates subjected to periodic in-plane boundary loading, for various boundary conditions.

2. To verify experimentally the results obtained from the theoretical analysis.

3. To draw conclusions from the experimental data and if necessary reconsider or modify the theoretical analysis.

To: Committee for NASA Research Proposals

From: Nicolaas Willems

Date: July 21, 1965

Re: Proposal for "Investigation of Dynamic Stability of Stiffened Plates subjected to Pulsating Loading"

In accordance with your request I herewith submit a breakdown of item 2 of the proposed Budget

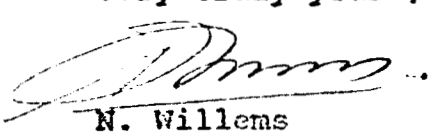
Item 2

a) Specimens, accurately milled plates:	estimated at 10 x $50 =	$ 500.00
b) Test frame to provide the different boundary conditions (simply supported, fixed and free):	estimated at	500.00
c) Periodic Loading Device (tentatively hydraulic) to produce various types of periodic loading (sinusoidal, square wave, triangular):	estimated at	1000.00
d) Strain and load recording equipment; gages, transducers, wires, etc:	estimated at	400.00
e) Miscellaneous (possibly additional recording equipment):	estimated at	600.00
	Estimated Total	$3000.00

No breakdown was given initially because the type of experiment (i.e. the boundary conditions and types of loading) will depend on the results obtained from the theoretical analysis and in how far the theoretical conditions can be realized experimentally.

Trusting that the above information will be of help, I remain

Very truly yours,



N. Willems
Associate Professor
Civil Engineering

THE UNIVERSITY OF KANSAS
LAWRENCE, KANSAS

DEPARTMENT OF PHYSICAL EDUCATION
AND RECREATION
Physiology of Exercise Lab

August 2, 1965

Aerospace Committee
School of Engineering
Campus

Dear Sirs:

As a result of project 40T, it is felt that telemetering technique of securing pulse rates with a minimum interference on men during strenuous exercise, that satisfactory transmission and pick-up can be secured while subjects are swimming.

With the transmitter outside of the tank, we have secured satisfactory readings with subjects emersed in a tank of water. It is believed that satisfactory pulse rate pick-up could be accomplished by placing the transmitter in a water proof container which would be worn on the subject's back.

Please consider this as an application for a grant in the amount of $1,740.00 to finance such a project as follows:

One Student Assistant @$125.00 per month - 9 months...	$1125.00
One Student Asst. 15 hours per week @1.00	540.00
Batteries and other supplies.....	75.00
Total	$1740.00

Sincerely yours,

Edwin R. Elbel, Professor
Physical Education

ERE:ee

Project CRES 40T - Telemetering Pulse Rates of Men During Exercise.

Project Director - Edwin R. Elbel.

Equipment - A transistorized transmitter approximately 1½" x 2" x 3", worn in a pouch on the subjects back is used as a transmitter. Pulse beat impulses are secured by affixing electrodes to the subject. The pick-up is accomplished by means of a FM radio. Recordings are made by means of a Sanborn cardette.

Experiments with respiratory rate of active men has proven disappointing in that it has been impossible to eliminate interference.

Satisfactory pulse rate recordings have been secured on subjects while doing strenuous work.

The problem of interference by FM stations has been practically eliminated by adjusting the antenna length to the desired frequency. The semi-rigid antenna has caused less interference than the thin wire "pig-tail" antenna.

On exercising men, it is necessary to eliminate the interference caused by muscle action and that which is caused by perspiration. The proper placement of the electrodes is very important in this respect. For most subjects the placing of one electrode on the upper extremety of the sternum slightly below the sterno-clavicular articulation and the other at the lower part of the sternum proved satisfactory. In the event, that the subject has a depressed sternum the lower electrode can be attached to the chest at the point of the "apex beat". The exact position of the third (reference electrode) is not important, at the center of the upper back at either side of the spinal column has proven satisfactory.

Perspiration interference has been largely prevented by using extreme care in affixing the electrodes. The skin at the desired point is thoroughly cleansed with alcohol after which the area around the point of contact is sprayed with a commercial athletic training-room substance named "Tufskin". The exact contact point is protected from the spray by small tape-discs. The discs are removed when the spray has dried. The electrodes-plastic button-sized discs with a silver electrode at the center, are then glued to a larger "doughnut-shaped" disc (about one-half inch in diameter) of foot-pad material "Kurotex". A small amount of electrode paste is in the center of the electrode.

After affixing the electrode, the outer edges of the Kurotex disc is "painted" with collodium. Satisfactory tracings have been secured while the subject is seated in a tank of water.

Attached are sample tracings. Each "spike" is, of course, a heart beat.

Heart Rate While Stair Climbing
Field House. 146/min.

Heart Rate - Running Up and Down
Steps Field House. 162/min.

THE UNIVERSITY OF KANSAS
SCHOOL OF PHARMACY
LAWRENCE, KANSAS
66045

September 3, 1965

Dr. William P. Smith, Chairman
Institutional NASA Grant Committee
School of Engineering
University of Kansas
Lawrence, Kansas

Dear Dr. Smith:

I am pleased to enclose my research proposal on "Behavioral Effects of Drugs under Limited Sensory Stimulation" for the consideration of support from Institutional NASA Grant. I presume that you need a proposal written to include essential objectives and the experimental program and not intended to be a literature review on the subject.

I am enclosing six copies for the distribution among your colleagues. A list of research publications with pertinent papers encircled is also attached with every copy. In case you need any further information, I will be pleased to provide the same immediately.

I will look forward to hearing from you in this regard.

Sincerely,

Harbans Lal
Associate Professor

HL:ab
Enclosure

Research Proposal

on

BEHAVIORAL EFFECTS OF DRUGS UNDER LIMITED SENSORY STIMULATION

Submitted

by

Kanhaiya Lal, Ph.D.
Associate Professor of Pharmacology and Toxicology
School of Pharmacy, University of Kansas

Introduction

During the prolonged flights and lunar explorations, astronauts will be subjected to varying degrees of 'sensory deprivation', as a result of confinement, limited activity, repetitive and monotonous routine and reduced overall sensory input. In addition the astronauts will frequently make use of drugs because a number of physical and physiological consequences of space flight appear unlikely to be resolved by engineering methods alone.

Recent research has indicated that mental alertness and functioning depends on continuous input of a variety of sensory stimuli. When the sensory input is reduced, it results into an increased irritability, boredom, fatigue, hostility, mental aberrations, hallucinations; and a definite loss in efficiency of mental performance, reliability, motivation and competence. The symptoms persist for sometime even after the sensory deprivation is discontinued.

It is known that drug action is influenced markedly by the environmental variables. There is some evidence that sensory stimuli imposed by the presence of another organism in the environment of an animal constitute a significant variable much the same way as light, sound, or heat; and may therefore influence the drug action profoundly. (Amphetamine ingested during space flight produced several unexpected pharmacological effects). It is therefore proposed to initiate systematic research into the effects of limited sensory input of the pharmacological actions of CNS drugs to understand their

biochemical mechanisms.

The immediate objective of the proposed study will be to investigate susceptibility of behavioral abnormalities induced by sensory deprivation to known pharmacological agents. In other words, is the performance of a given response more or less vulnerable to the effects of drugs when the response is tested at different drive levels provided by sensory stimuli of varying degrees? Enhancement or the decline in performance by drugs will be significant information for this study.

Experimental

The objective of the experimental program will be initially limited to the measurement of operant behavior of normal and drug treated rats in presence as well as in absence of social stimuli of varying type and duration.

The operant behavior will consist of lever pressing response in a Skinner box. Through proper reinforcement schedules the behavior of the animals will be put under the control of known antecedents and the behavior thus emitted will be quantitatively recorded as number of correct and incorrect responses per unit time. The reinforcement will include water, food, brain self stimulation or shock avoidance.

The rats will be deprived of social stimuli for varying periods before and during training or testing. Social stimuli when provided will consist of a companion rat in the same cage. The companion rat will perform one of the following functions:

1. Audience. An instrumentally naive rat acting just as a passive spectator in the cage.
2. Co-action. The companion rat will be engaged in same activity at the same time, and in full view of each other. But the activity of one will not benefit the other in any known way. For example, one rat may press lever to get water while the other may press lever to get electric shock through an implanted brain electrode.
3. Co-operation. The companion rat will be engaged in an activity which will provide the experimental subject with cues or information as to the appropriate behavior. For example, one rat may press a lever to turn on a signal in the presence of which the other rat may press a lever to get reinforcement. In other instance, one rat may be trained to press a lever to turn off a grid shock enabling the other rat to press lever to get reinforced.

The rats will be trained independently for operant conditioning. During testing, two randomly selected rats will be placed in a cage with both contingencies.

The drugs will be administered in appropriate doses by and appropriate route. The control rats will be injected with saline. The treated rats will be tested for operant behavior after several predetermined post injection periods. The data will be analyzed statistically. A tentative list of drugs of interest for this study includes amphetamine,

chlorpromazine, carbachol and atropine.

Significance

The results obtained from this study will provide evidence concerning the type and amount of sensory stimuli necessary for omission of normal behavior as well as the usual drug action. In addition it may lead to an understanding which will aid in predicting the drug effects under space flight conditions or in devising pharmacological means to prevent the mental and physical deterioration of astronauts. It will provide preliminary data necessary to initiate investigation on biochemical basis of mental aberrations produced by sensory deprivation.

Budget

Salaries	
Research assistant 1/2 time - 11 months	$2,689
Supplies	
Drugs, animals, animal feed, expendable electronic parts, etc.	400
Publication Cost	50
TOTAL -	$3,139

TITLE OF PROJECT: Cardiovascular Responses Under "Zero-g" Conditions Simulated by Reducing Sensory Input.

INVESTIGATOR(S): Floyd E. Leaders, Jr., Assistant Professor of Pharmacology
Department of Pharmacology
University of Kansas Medical Center

Stata Norton, Associate Professor of Pharmacology
Department of Pharmacology
University of Kansas Medical Center

BUDGET REQUEST:

Item	Requested
1. Personnel	
Principal Investigators	none
Technician, part time (Retirement, etc., not included)	$2500.00
2. Permanent Equipment	
Apparatus for recording blood pressure of conscious rats.	$ 100.00
3. Consumable Supplies	
Animals (rats)	$1600.00
Animal care (chronic animals)	$1400.00
Chemicals, drugs, recording paper, publication costs, etc.	$ 400.00
4. Travel (Not included in this budget)	none
	$6000.00

2 yr plan 10 mos

Principal Investigator(s):

Floyd E. Leaders, Jr., Ph.D.

B.S. Pharmacy, Drake University, Des Moines, Iowa, 1955.
M.S. Pharmacology, State University of Iowa, Iowa City, Iowa, 1960.
Ph.D. Pharmacology, State University of Iowa, Iowa City, Iowa, 1962.

Positions:

Instructor, Pharmacology, University of Kansas Medical Center, 1962-1964.
Assistant Professor, Pharmacology, University of Kansas Medical Center, 1964-present.

Primary Interests:

Autonomic, Cardiovascular Pharmacology and Physiology. Non-erythroid properties of Erythropoietin.

Organizations:

Aerospace Medical Association
American Society for Pharmacology and Experimental Therapeutics

Publications:

1. Mechanism of the Positive Chronotropic Response to Nicotine. Floyd E. Leaders and J. P. Long. J. Pharmacol. 137: 206-212, 1962.

2. Action of Nicotine on Coronary Vascular Resistance in Dogs. Floyd E. Leaders and J. P. Long. Amer. J. Physiol. 203: 621-625, 1962.

3. The Cholinergic Component in the Sympathetic Innervation to the Spleen. Floyd E. Leaders and Conrado Dayrit. J. Pharmacol. 147: 145, 1965.

4. Separation of Adrenergic and Cholinergic Fibers in Sympathetic Nerves to the Hind Limb of the Dog by Hemicholinium (HC-3). Floyd E. Leaders, J. Pharmacol. 148: 238, 1965.

5. Mechanism for Nicotine and DMPP on the Isolated Rat Atria-Vagus Nerve Preparation. Tzu-sung Chiang and Floyd E. Leaders, J. Pharmacol. In press, Sept, 1965.

Previous Work Supported from NASA Research Grants NSF-298, CRES 40-G, $3200. - Elucidation of Cell Growth Stimulating Properties of Erythropoietin. Floyd E. Leaders and A. A. Werder.

Publications:

1. Erythropoietic Stimulating Factor (ESF) as a Stimulant of Cell Growth In Vitro. Floyd E. Leaders, Alvar A. Werder and Charlotte Schmidt. Proc. Soc. Exp. Biol. and Med. 115: 658-660, 1964.

2. Mesenchymal Metaplasia of the Chick Chorioallantoic Membrane; A Non-Specific Response to Selected Stimuli. Robert R. Rich, Don K. Rogers and Floyd E. Leaders. Experimental Cell Research - In Press.

3. Erythropoietic Stimulating Factor (ESF) Associated with an Oncogenic Virus-Host System In Vitro. Floyd E. Leaders, Alvar A. Werder, Charlotte Schmidt and Mary-Lucille Castro. Proc. Soc. Exp. Biol. and Med. - Submitted.

Abstracts:

1. The Effects of Selected Stimuli on the Chick Chorioallantois. Robert Rich, Don Rogers and Floyd Leaders, Fed. Proc. 24: 555, 1965.

2. Erythropoietic Stimulating Factor (ESF) Associated with an Oncogenic Virus-Host System In Vitro. Floyd E. Leaders, Alvar A. Werder, Charlotte Schmidt and Mary-Lucille Castro. Pharmacologist 7: 180, 1965.

This work was the basis for an independent NIH Grant proposal No. CAAI 08569-01 now under consideration by NIH for funding as of Feb. 1, 1966.

Stata Norton, Ph.D.

B.S. Zoology, University of Connecticut, Storrs, Conn., 1943.
M. A. Zoology, Columbia University, New York, New York, 1945.
Ph.D. Zoology, University of Wisconsin, Madison, Wisconsin, 1949.

Positions:

Neuropharmacologist, Wellcome Research Laboratories, Tuckahoe, New York, 1945-1947; 1949-1962.
Assistant Professor, Pharmacology, University of Kansas Medical Center, 1962-1965.
Associate Professor, Pharmacology, University of Kansas Medical Center, 1965-present.

Primary Interests:

Neuropharmacology, neurophysiology.

Organizations:

American Society for Pharmacology and Experimental Therapeutics
Ecological Society of America
Biometrics Society

Publications:

1. S. Norton and K. I. Colville. Antagonism of reserpine by intraventricular bretylium. Nature, 192: 72-73, 1961.

2. C. H. Ellis and S. Norton. Drug antagonism to CNS-induced arrhythmias. Excerpta Medica, Intern. Congress Series 48, 1962.

3. R. E. Jewett and S. Norton. Measurement of behavior of rats under isolation and observations on preliminary drug effects. Psychopharmacologia, 6: 151-158, 1964.

4. R. E. Jewett and S. Norton. Effect of 8-azaguanine on learning of a fixed interval schedule. Nature, 207: 277-278, 1965.

5. S. Norton and R. E. Jewett. Frequencies of slow potential oscillations in the cortex of unrestrained cats. Electroenceph. clin. Neurophysiol. 19: 377-386, 1965.

RESEARCH PROPOSAL

Background Material:

The effects of weightlessness on the circulatory system are of interest due to observations available after both short and prolonged orbital flights of the astronauts. Available information on medical evaluation of astronauts has indicated that orthostatic hypotension and tachycardia may be present for some time post flight (1). However, these effects apparently were less pronounced following the 8 day orbital flight of Gemini 5 (2). This has been attributed to a physiological adaptation of the body. However, an alternate explanation is equally possible. Since the capsule was tumbling during the power-down portion of the flight this factor may have resulted in an increase in sensory input as discussed in the hypothesis presented below.

Confinement (3,4), prolonged bedrest (5), and the buoyancy effect of immersion in water (6,7) have all been used to simulate the effect of "zero-g" in ground-based studies. The similarity between the effects of "zero-g" on the cardiovascular system and these forms of restriction of physical activity has been demonstrated (1).

Many hypotheses have been proposed to explain the cardiovascular changes resulting from these experiments on sensory restriction and from orbital flight situations (4,8). All of these proposals, however, are based primarily on research concerning only the peripheral autonomic system.

That centrally originating pathways exist which control peripheral vascular responses is widely accepted (9,10). However, the role of the CNS in influencing vascular responses under the condition of real and simulated "zero-g" has been largely ignored. In addition to the CNS control of the vasculature, sensory input to the CNS should be considered as a factor in a feedback system consisting of afferent input: CNS: autonomic nervous system regulation. Alteration of sensory input is known to have marked effects on the CNS (11). Since any ascending sensory tract can be considered to affect the CNS via reticular formation connections (12), this may be expected to apply to all polysynaptic pathways involving proprioception (13). Thus, a major source of sensory input to the CNS may be mediated through nerves carrying proprioceptive impulses from skin, joints and muscles. Fibers carrying these impulses constitute a large portion of the dorsal root afferent fibers of all segments of the spinal cord. The effect of real and simulated "zero-g" on sensory input from these pathways has not been evaluated critically.

Total peripheral resistance of blood vessels is under the influence of the degree of vasoconstriction (tone) and the character of vasomotion (14). The importance of vasomotion in the total control of circulation is apparent when one considers the large cross sectional area of the capillaries compared with the area of the larger vessels of the cardiovascular system.

Based on this information, the following hypothesis is proposed.

Cardiovascular symptoms following "zero-g" are due to alteration of peripheral vasomotion with consequent inadequate venous return. Further, this phenomenon is brought about by altered CNS activity due to decreased sensory input from proprioceptors resulting from lack of "normal" gravitational influence.

The purpose of this proposal is to initiate pilot studies to test this hypothesis.

Experimental Procedure:

1. Effects of spatial confinement on microcirculation using anesthetized animal techniques.

Two large groups of rats will be used. Each group will be subdivided to evaluate the effects of confinement at the time intervals of 2, 4, 6 and 8 weeks. The control groups will be simultaneously studied at similar intervals. Confined rats will be maintained in cages of a size which will restrict movement to feeding and leg movements. Control rats will be kept in groups allowing free movement in normal sized cages.

At the time of the experiment, animals will be anesthetized and the following parameters observed:

a. EMG (Electromyogram): to determine level of muscle function.

b. Vasomotion: by direct vital microscopy. Evaluation of frequency of vasomotion in rat mesentery will be done using standard techniques (15,16).

c. Systemic blood pressure: by tail cuff.

Statistical analysis will be performed on the data obtained to compare confined and control populations.

2. Development of techniques to allow microcirculation studies in unanesthetized rats.

Some techniques are available using other species for observing microcirculation responses in unanesthetized animals. These species, such as the rabbit and bat do not lend themselves readily to studying differences between confined and non-confined animals. The techniques for vital microscopy which may be used include transillumination of original thin tissues, incident illumination of surface capillaries, observation of original or regenerated thin tissue in a chamber and transillumination of a thin section of original tissue with a light conducting rod. Transillumination through a prepared chamber has even been applied to humans (17).

The proposed work will include chronic implantation of lucite "windows" using several peripheral beds such as the skin flap on the back of the neck. Chronic implantation of EMG electrodes will be attempted for use simultaneously in these animals. EKG will simultaneously be recorded.

Using the above developed techniques, groups of restrained animals similar to those designed for section 1 will be tested without anesthesia and the responses will be compared both with those of unanesthetized controls and with responses recorded for group 1.

3. Perfusion studies.

The perfused hind end of the rat will be used (18) to evaluate total peripheral resistance in rats which have been subjected to conditions of confinement. A positive correlation is expected between effects of confinement on total peripheral resistance as determined by perfusion experiments, on microcirculation by vital microscopy, and on EMG.

Experimental groups and timing of experiments will be similar to the schedule outlined in section 1.

4. Spinal cord section.

Another mechanism of decreasing sensory input or simulating "zero-g" is to remove a major portion of afferent input by spinal cord section. Standard techniques for low cervical or thoracic section will be used. These animals will be chronically maintained as long as feasible depending on overt condition of the animal. Animals will be tested at 2, 4, 6 and 8 week intervals if possible.

Vital microscopy, EMG, EKG, systemic blood pressure and hind limb perfusion studies will be performed on these animals as described previously.

5. Attempt to offset these effects by providing sensory input by constant movement of the animals.

If significant differences in cardiovascular function arerecorded as expected between control and experimental animals above, an attempt will be made to counteract this effect. Confined animals will be placed on a horizontally moving platform which will shift the animals' weight at a fixed frequency. These animals will be compared with non-moved animals according to the time schedule outlined in section 1. If the hypothesis is valid, a return toward normal cardiovascular response would be expected to be brought about by this treatment.

These studies are intended as a preliminary investigation to evaluate the hypothesis presented. Should these experiments prove the feasibility of such an approach to the cardiovascular responses to simulated "zero-g" conditions a proposal for full scale sponsored research will be submitted to NASA before the termination of this pilot study.

REFERENCES

1. Lamb, L. E.: Aerospace Medicine 35: 413, 1964.

2. Radio and Television News Coverage, Gemini 5, Time Magazine, Sept. 10, 1965.

3. Lamb, L. E., Johnson, R. L., Stevens, P. M. and Welch, B. E.: Aerospace Med. 35: 420, 1964.

4. Bonfils, S., Liefooghe, G., Gelte, X., Dubrasquet, M. and Lambling, A.: Rev. Franc. Etudes Clin. et Biol. 15: 1096, 1960.

5. Taylor, H. L., Henschel, A., Brozek, J. and Keys, A.: J. Appl. Physiol. 2: 223, 1949.

6. Graveline, D. E., Balke, B., McKenzie, R. E. and Hartman, B.: Aerospace Med. 32: 387, 1961.

7. Graveline, D. E. and McCally, M. Aerospace Med. 33: 1281, 1962.

8. Johnson, P. C.: Circulation Res. 15: 2, 1964.

9. Uvnäs, B.: Handbook of Physiology, Section 1: Neurophysiology, Volume II Ed. John Field, Williams and Wilkins Co., Baltimore, 1960, page 1131.

10. Beck, L.: Texas Rep. on Biol. and Med. 22: 375, 1964.

11. Solomon, P. (Ed.). Sensory Deprivation. Harvard Univ. Press, Cambridge, Mass., 1961.

12. Magoun, H. W. The Waking Brain. C. C. Thomas, Springfield, Ill., 1963.

13. Glees, P. Experimental Neurology. Oxford University Press, London, 1961.

14. Lutz, B. R. and Fulton, G. P.: Factors Regulating Blood Flow, Ed. G. P. Fulton and B. Zweifach, Amer. Physiol. Soc., Washington, 1958, page 13.

15. Zweifach, B. W.: Functional Behavior of the Microcirculation. Charles C. Thomas, Springfield, Ill., 1961.

16. Nicoll, P. A.: Circulation Res. 15: 245, 1964.

17. Brånemark, P. I., Aspegren, K. and Breine, U.: Angiology 15: 329, 1964.

18. Brody, M. J., Shaffer, R. A., and Dixon, R. L. J. Appl. Physiol. 18: 645, 1963.

UNIVERSITY OF KANSAS MEDICAL CENTER

RAINBOW BOULEVARD AT 39TH STREET
KANSAS CITY 3, KANSAS • TA 2-5252

DEPARTMENT OF PHARMACOLOGY

September 15, 1965

Dean W. P. Smith, Chairman
Interdisciplinary Committee on Space Science
and Technology
116 Engineering Building
University of Kansas
Lawrence, Kansas

Dear Dean Smith:

The purpose of this letter is to request short term funds to facilitate preparation and submission of a multidisciplinary grant proposal to the National Aeronautics and Space Administration. The proposal is outlined briefly in the attached summary.

Several considerations have been taken into account to justify this request. These are:

1. This proposal is of a magnitude large enough to constitute a true university-wide multidisciplinary facility. Hence, it falls within the realm of the Interdisciplinary Committee on Space Science and Technology.

2. Justification cannot be found for requesting any single department or even a group of departments to bear the expense of preparing such a proposal.

3. Funds requested will enable hiring of an assistant (part-time) to the proposed project director. This assistant will be capable of carrying out the time consuming work involved in formulating this application without bringing an undue hardship on any department of the university.

The following funds are requested for the period from November 1, 1965 to June 30, 1966:

Personnel:

Assistant to act as librarian, secretary, etc. and perform other tasks in preparation of this application	$ 2000.00
F.I.C.A. and Retirement	165.00

Consumable Supplies:

Phone calls, secretarial supplies, printing costs	300.00

Travel:

To Washington, D.C. to talk to N.A.S.A. if warranted	500.00
	$ 2965.00

A moderate amount of travel funds has been included on the advice of individuals who have sought and obtained NASA funds previously.

Support for this application has already been obtained from a number of local faculty members and further support is being solicited at the present time. This phase of the project will be completed prior to the November 1, 1965 starting date of this request. If sufficient interest has not been demonstrated by that time by the present faculty the request for funds will be withdrawn.

This request is for a period of eight months. If the application is still pending at that time, a further request will be presented then if it is justified. If the negotiations concerning this grant should cease any time during these eight months due either to NASA or KU rejection, work on this portion will be terminated and the remainder of the unused funds will be transferred back to the committee.

The proposal which will be submitted to NASA is a product of the University of Kansas Medical Center Space Biology Study Unit. Several months of consideration and effort preceded its inception. The final decision to ready this proposal for submission at this time was reached in response to the recent encouragement of Col. H. B. Webb. Col. Webb is a former member of the KUMC Space Biology Study Unit and played an important part in the design of the present program. He is now in the Office of the Surgeon General in Washington, D. C. and can undoubtedly be of assistance in negotiations concerning the proposal. It is felt that a program of the type which will be submitted will have a very good probability of receiving funds. If additional information is necessary, or if a personal appearance before the committee is desired, please contact me.

Sincerely,

Floyd E. Leaders, Jr., Ph.D.
Chairman, KUMC Space Biology Study Unit

Department of Pharmacology
University of Kansas Medical Center
Kansas City, Kansas

Russell C. Mills, Ph.D.
Associate Dean
University of Kansas Medical Center
Kansas City, Kansas

FEL/ir

PROJECT TITLE:

Establishment of a Colony of Small Mammals for Studies on Long Term Biological Effects of Space Environment.

Principal Investigator (Project Director):

Floyd E. Leaders Jr., Ph.D.

Assistant Professor of Pharmacology

TOTAL DURATION OF PROPOSED PROJECT:

July 1, 1966 to June 30, 1976 and beyond.

PERIOD OF INITIAL REQUEST FOR FUNDS:

July 1, 1966 through June 30, 1968 (24 months) with subsequent stepwise funding negotiated yearly.

AMOUNT OF THIS APPLICATION:

Year 1, $ 110,000*

Year 2, $1,100,000*

*These are rough estimates and cannot be entirely accurate since costing has not been completed and cannot be at this stage. Year 2 includes beginning construction of a physical plant. The estimates will most likely prove to be conservative.

SUMMARY OF PROPOSAL

PROPOSAL:

The University of Kansas proposes to conduct a project for selecting, raising and analyzing a population of mammals (mice) for ultimate research in space. The proposal is designed to enable the long term evaluation of large numbers of parameters under a large variety of environmental conditions initially using ground based facilities and later in-flight experiments.

DISCUSSION

Background:

Equipment now in the design phase or better is capable of placing man on the moon and nearby planetary bodies. Space provides great advantages to research in many fields and astronomical observatories, particle accelerators, biological laboratories and other such items of large equipment will eventually be located in space. These activities will undoubtedly require long periods of human staffing.

The acute reactions of selected mammals, including man, to some of the stresses of extraterrestrial operations are known and will be even more adequately understood within the next few years. However, the long range adaptations are still speculative and the possible developmental or evolutionary consequences of extraterrestrial colonization on a population of mammals, including man, are even more hypothetical. We cannot plan the eventual inhabitation of space without a fundamental knowledge of the possibilities which will be faced.

Objective:

A colony of mammals (mice) has been chosen to obtain information of this nature. To establish such a population is itself a multidisciplinary research and development project, but is not itself the objective of this proposal. The objective is to provide a population of mammals and controls upon which a wide variety of scientific disciplines can make observations, design experiments and draw samples or specimens. The objectives of the proposal herewith submitted, then, is

to establish a research instrument which can serve science generally. This instrument will allow distribution of knowledge, biological material and eventually whole animals to the interested scientific community of the free world for study of the effects of the "space environment" on these animals.

Examples of the potential use which can be made of such an instrument are many. It will be possible to make available to behavioral scientists controlled groups of subjects to test and observe under both earth conditions and those of "space". It will be possible to provide geneticists with known strains of known genetic variability, and specimens to examine. Embryologists and pathologists can have serial specimens of gravity-unstressed ova, embryos, fetuses, infants and adults for examination. Pharmacologists, physiologists and biochemists will have animals in which the long term effects of a "space environment" can be studied on responses to drugs, enzyme systems and physiological mechanisms. Endocrinologists, radiologists and most other life-scientists will be able to design and carry out experiments with this population. From such work much can be learned about life processes and about the potentialities and limitations of biological systems in space.

Choice of Animals:

The mouse has been chosen for the following reasons:

1. A knowledge of long-term effects can be obtained on a compressed time scale.
2. A large body of information is available.
3. Many strains and special types of mouse are available.
4. We have a good knowledge of the applicability of mouse data to man.
5. The logistics are within the weight and balance capability of existing and contemplated space systems.

Populations to be Established:

To make the in-flight studies meaningful, there will have to be several control populations of mice on the ground. Groups which will be established will be:

1. A population raised in a natural earth environment.

2. A population raised on the ground in a simulated space cabin environment.
3. An axenic (germ-free) population raised on the ground in a simulated space cabin environment. This group could become extremely important when mankind ultimately reaches planetary bodies which potentially could support endogenous biological environment.
4. Population 2 in-flight situations.
5. Population 3 in-flight situations.

By the use of statistically large and well controlled populations during the ground phase of the proposal, the number of animals which must be observed and maintained in the space environment will be smaller. Since weight and space limitations will be a problem initially, this design will allow a return of information for preliminary evaluation prior to the establishment of a permanent population of mammals in space.

Method of Procedure:

1. Collection of information concerning mice.
2. Select or create a strain of mice.

This strain of mice will be selected or bred to have characteristics believed to provide the maximal amount of useful information in the opinion of the various branches of the life sciences.

3. (a) Genetically stabilize population.
   (b) Design experiments to be performed.
4. (a) Begin collection of data from earth environment population.
   (b) Design and construction of non-biological aspects of space environment simulator facility.
5. Begin collection of data from ground based simulated space environment population.
6. Begin collection of data from axenic population.
7. Collaboration with in-flight programs to integrate mouse populations into vehicles.

8. Begin collection of data from in-flight populations.

Role of the University of Kansas:

1. Establish a central registry of information concerning:
   (a) Mice - strains, characteristics, etc.
   (b) Relevant research elsewhere.
   (c) Research workers in this and closely related fields.
2. Preparation of mouse population.
3. Design and development of non-biological aspects of program.
   (a) Gathering of information on and begin work on simulators and equipment needed.
   (b) Adaptation of equipment available and design of equipment for use on this proposal.

Phase 3 of this section relies heavily on an interdisciplinary approach involving the medical science, life science, engineering science, and physical science departments of the University.

4. Training of pre- and/or post-doctoral fellows in both biological and non-biological areas of the project.

   Implicit in this project is one of the major roles of the University, training of future research personnel. The selection of a university to establish this population of mammels facilitates a coordinated dual program of research and training. This entire proposal will be implemented within the established framework of the university. For this reason it lends itself readily to the concurrent training of both predoctoral and postdoctoral fellows. Research and graduate work in one of the medical science, life science, engineering science or physical science departments involved in this project would provide scientists well oriented and extremely capable of pursuing a career in one of the areas of space research. A program for the training of a number of these people is incorporated in this proposal.

5. Design and building of physical plant facilities funded by this program on University of Kansas land.
6. Coordinate selection of experiments to be done.
   (a) In-house projects.
   (b) Projects to be done elsewhere.
7. Initiate approved research projects.
   (a) In-house research by associated faculty and personnel. These projects to be funded from this proposal.
   (b) Coordinate research projects approved for other research institutions. These projects to be funded from other sources.
8. Coordinate in-flight program with NASA organization in charge of flight program for various orbital laboratories or other vehicles.
   (a) Coordinate distribution of in-flight specimens in relation to section 7 (a) and (b).
9. Preparation of facilities to allow similar research to be accomplished using larger mammals when physical limitations will allow this.

The functions of the University of Kansas listed above will be handled by the university within the existing curriculum and departmental framework. Laboratories to be used initially and future laboratories to be built using funds from this project will also remain within this existing framework.

CONCLUSION

It is considered that this project stands on its own feet as a necessary requirement of the general scientific community. The advancement of the life sciences is going to require ultimately a population of experimental animals in space. When this is to be done physically, inclusion of uncontrolled animal stock will be a waste of time, money and valuable in-flight space. Little usable information will be obtained if at that time the research workers just take along a clutch of guinea

pigs, rats, monkeys or other animals. The sciences will need experimental animals about which as much baseline or control data as possible are already known, and it will need enough of them so that statistically significant numbers of observations can be made, tests performed, samples analyzed or specimens examined. This project will provide the instrument to fulfill this requirement. In order to have this instrument ready when the physical techniques are ready to place it in orbit, the project should be started now or in the very near future. Otherwise, as was previously stated, we will be wasting our own time and energies in space on experiments having no validity. If the project can be started now it will be ready and can be adapted to presently proposed programs and to whatever space programs will be in progress in the '70's.

October 19, 1965

To: NASA Interdisciplinary Committee

From: B. G. Barr, Assistant Professor - Mech. Eng.
R. R. Gatts, Professor - Mech. Eng.
C. B. Saunders, Professor - Business Adm.

Subject: Information Retrieval

Objectives

1.) To survey possible computerization of space related reports not now on computer tapes.

2.) To develop computer routines for retrieving bibliographic data on NASA or space related reports.

CRES Project 60-M (Technology Utilization) personnel have found that regional industry can be helped by supplying information on specific problems. The 66 literature searches performed have confirmed earlier suspicions that manual searching of the thousands of NASA reports is unfeasible. Indiana University (ARAC) has been providing Project 60-M with bibliographies compiled by computer, but these bibliographies have often deviated from the subject in question. Three to six weeks are required to obtain the results of the computer search. Few companies appreciate more than a month's delay in locating information on a problem. By having a computer search capability at K.U., results would be available at least two weeks sooner. Although information on many topics can be found in non-IAA or NASA sources, the detailed specific data which is often essential can usually best be found in space oriented material.

To date Project 60-M personnel have contacted 108 regional industries in their efforts to develop an effective information transfer mechanism. If the present ratio of search requests to companies contacted is any indication of potential, Kansas' 4,000 industries have at least 2,500 search requests. Experience has shown that answers to one question generate further questions and consequently further search requests. The Guide to the World's Abstracting and Indexing Services in Science and

Technology lists some 400 distinct abstracting services. To provide a truly complete bibliography, probably 100 of these indexes would have to be consulted.

It is proposed that a computer programmer or student assistant work closely with Project 60-M personnel to develop computer programs for existing NASA & IAA tapes. By participating in existing searches, and observing the operations of Wayne State, Indiana University, and the University of Pittsburgh, the programmer would gain a thorough knowledge of problems and procedures. It is hoped that the experience of 60-M members would help in establishing more selective computer programs than are used by Indiana University. Once suitable programs were developed for the NASA tapes, the 60-M engineers could identify indexes which warranted taping.

The effort proposed would accomplish the following:

1.) Initiate the development of a computer based search capability at K.U.

2.) Provide information, data and experience necessary to prepare a sound proposal to NASA or Kansas Research Foundation (Technical Services Act) for establishment of a search facility.

3.) Give immediate assistance to Project 60-M engineers on search requests for industry.

Proposed Budget (Jan. 1, 1966 to Dec. 30, 1966)

Graduate Student (1/2 time 9 mo.; F.T. 2-1/2 mo.)	$2,800
Travel to Wayne State University, University of Pittsburgh, Indiana University	500
	$3,300

RESEARCH PROPOSAL

TITLE: Methods of Generating and Taking Data on a High-Speed Random Bit Source with Equal Transition Probabilities

PERSONNEL: John N. Warfield, Ph.D.; Advisor
Herschell F. Murry, M.S.; Research Assistant

TIME PERIOD: Spring Semester, 1966

BACKGROUND

Much is to be found in the literature on the use of random numbers and on random binary numbers in particular. Little is to be found, however, on methods of obtaining these numbers. Thus it seems that to verify the many theories evolved, as well as to develop a useful tool for future work, an approach for realizing such a binary number generator and guaranteeing its randomness is needed.

In order to be fair in our assessment of the literature on the generation of random numbers, we must say that tables of "random" numbers have long been available, as are the more recent digital computer programs for generating "random" numbers. Tables of random numbers do not, of course, lend themselves to modern automatic computation equipment and have a limited number of combinations so that any randomness is eventually cyclic. Even more important is the fact that tables of numbers are necessarily derived and manipulated by humans and are subject to human biases as discussed long ago[1] by M. G. Kendall and B. Babington Smith.

As for the computer-generated random numbers, they also have several faults. Although it is realized that these numbers have many uses, they have the following shortcomings:

A. The same sequence of numbers is generated from the same starting number.

B. The numbers repeat cyclically so as to be unsatisfactory for use in problems of long computational duration.

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1. "Randomness and Random Sampling," J. Royal Statistical Society, vol. 101, 1938, p. 151

C. The computations required for generating such a number within a digital computer is often several times as involved as the computations required by the problem actually being solved. This needlessly over-complicates the machine.

D. Due to the time required for generating each random number, the remainder of the computer must wait idle for significant portions of the total computation time. Estimates[2] of one to two orders of magnitude of increased computation speed have been made for a machine with an independent number generator derived from a natural noise source.

From these comments we can infer the basic reasons for wanting to generate a random binary number:

1. True randomness is possible.
2. Random numbers in any number system may be derived from the random binary number generated.
3. Computational speed can be increased.
4. Equipment costs may be minimized in many instances due to decreased complexity.
5. Theory now residing in the literature may actually be proved and a research tool created.

In obtaining a random bit, we have two states ("1" and "0") which should be equiprobable if the bit is truly random. Upon sampling the bit at equally spaced intervals, we have the following probabilities at sample time n: $P(0_n/0_{n-1})$, $P(0_n/1_{n-1})$, $P(1_n/1_{n-1})$, and $P(1_n/0_{n-1})$ where the state below the fraction bar is the previous state. Thus we have the four state transitions possible, which are read "probability of entering state _____ given the previous state _____." These are called transition probabilities and must all equal one-half if the random bit sampled is to be equally likely of being a "1" or a "0".

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[2] W. Lansdown, "Random Walk Solution of Laplace's Equation: Method and Machine," Ph. D. Thesis, The University of Kansas, Lawrence, Kansas, 1964.

PROPOSED WORK

Initial stages of the work have already begun. The basic circuits for part A, below, have already been built, inter-connected, and operated. The chronological plan of attack is as follows:

A. Low-speed (< 1 megacycle) sampling of a random flip-flop driven by a commercial random noise source with measurements of the transition probabilities by analog integration and recording. As pointed out in earlier work[3], the data-taking equipment is an essential part of any random source and must be given early and adequate consideration. The sampling rate will be varied in order to verify expected limitations on the sampling rate.

B. Measurement of the same probabilities on the same circuits as in part A by digital means and performance of tests on the results with the digital computer.

C. Incorporation of any changes indicated by prior data into an all-micrologic test set running at its maximum speed (about 40 megacycles).

D. Recording and processing of data from high-speed micrologic circuits. These 40 megacycle circuits represent the state-of-the-art with respect to digital circuit speed. With further development of such devices as the MASER and LASER, we are on the threshold of much higher speed operation, which leads us into the next phase of the work.

E. Formation of theory for methods of quantizing the signal from a random noise source operating at UHF (300-3000 mc) and SHF (3000-30,000 mc) speeds. Radio frequency techniques,

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[3] H. F. Murry, "Generating and Taking Data on Stochastic Processes," University of Kansas Center for Research, Inc.; Lawrence, Kansas; Fall, 1962.

such as phase modulation, now common to the communications industry but not yet applied in the field of computation, are expected to yield fruitful results.

F. Construction of a UHF noise source and the circuits for quantizing its output. Data-taking in this region will be quite difficult[4] so that we can expect little more than observation of the desired results.

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[4] One second of random number generation at 1000 megacycles would require , for instance, about 24 hours of machine processing by today's fastest computer, assuming that we have some way of recording numbers generated at such a rate.

EQUIPMENT

QUANTITY	DESCRIPTION	PROCUREMENT
1	General Radio Noise Source	EE Electronics Lab
4	A.C. Voltmeter	" " "
1	High-Speed Electronic Counter	" " "
4	D.C. Voltmeter	" " "
2	D.C. Power Supply	" " "
1	Crystal Controlled rf Oscillator	" " "
1	rf Receiver	" " "
1	Four-Trace Tektronix Oscilloscope	EE Digital Lab
2	Dual-Channel Chart Recorder	EE Analog Computer Lab
2	X-Y Recorders	" " " "
	Digital Computer	Computation Center
1	Digital Magnetic Tape Recorder	" "
4	Solid-State Operational Amplifiers	Purchase, @$100 each
	Assorted Micrologic Circuits	Purchase, $300
2400 ft.	Computer Quality Magnetic Tape	Purchase, $60
	Assorted Hardware	Purchase, $240

Total Parts	$1000
Research Assistant @Full-Time Spring Semester	$2200
Total Allocation	$3200

I. Title of proposed research.

Evaluation of methods of numerical taxonomy in paleontology using selected species of Fusulinacea.

II. Time period for which support is requested.

June 1, 1966 through May 31, 1967.

III. Description of proposed research.

A. Purpose of research.

It is proposed to evaluate the techniques of numerical taxonomy to determine their applicability to populations of fossil organisms. Selected species of fusulinids, a group of extinct Paleozoic protozoans, will be used in the study. This research is envisioned as a pilot study. If the results are meaningful, a larger study, hopefully with non-university support, will be made encompassing a larger number of species of superfamily Fusulinacea.

Fusulinids are particularly well-suited for the proposed research. They are often abundant and well-preserved. Because they grow by adding chambers, they preserve their complete ontogeny; and this ontogeny gives an indication of their phylogeny. They are relatively simple, poorly organized organisms; but their shell is structurally complex and has many quantifiable morphologic characters.

B. Theoretical basis of research.

Crater density on Mars, as shown by photographs taken by Mariner IV, is much lower than would be expected if the surface of Mars were of great geologic age. Three independent investigations have indicated that the surface is only about 300 million years old and that before that time "a substantial amount of erosion on Mars in indicated" (Baldwin, 1965). The possibility of "liquid water and denser atmosphere [and thus, perhaps, life] during the first 3.5 billion years of its history" is not to be ruled out (Anders and Arnold, 1965, brackets mine).

If these conclusions are correct, then the probability of finding fossils on Mars is far greater than that of finding living organisms. Even if life were found, the study of its fossil remains will provide much evidence of its evolution that cannot be obtained by studying only living organisms.

Samples of extraterrestrial life or fossils, if collected at all, will be extremely spotty in the initial stages of exploration. It would be unfortunate if the Linnean System, originally designed for a non-evolutionary world, were to be used in the systematic study of this life. The Linnean System is not well-suited for use with very limited sampling, and it has the further disadvantages of requiring a hierarchical organization of nature and of being excessively typological. Finally, as modified to be consistent with evolutionary theory, it is a phyletic system. That is, classifications are designed to reflect the evolution of the organisms involved. Thus with each change in the concept of the evolution of a group of organisms, the classification is also changed with resultant confusion in the scientific literature.

More to the point in the study of a new natural system would be the application of one of the new quantitative taxonomic methods that emphasizes only the similarities among organisms (phenetic similarity) rather than supposed phylogeny (Sokal and Sneath, 1963). At present very little is known about the applicability of these methods to paleontology. The following questions are only a few of the ones still unanswered about numerical taxonomy and its uses:

1. To what extent does phenetic similarity of the fossilized shell material reflect phenetic similarity of soft parts?

2. Do methods of numerical taxonomy give meaningful information when applied to fossil collections from more than one geologic age with supposed continuous evolution?

3. What similarities and differences exist between the phenetic and supposed phylogenetic classifications of organisms?

4. What are some of the biologic/paleontologic causes of the similarities and differences listed in 3 above?

In order to answer these and other questions about the applicability of numerical taxonomy to the classification of fossils and to evaluate the use of these methods in the study of the systematics of extraterrestrial life, this research is proposed.

C. Objectives and expected significance.

Four questions fundamental to this research are:

1. How much variation do members of a single species show within one locality?

2. How much and in response to what factors do members of a single species vary over their geographic range?

3. Does numerical taxonomy provide a classification of organisms that is useful for stratigraphic work?

4. To what extent does a phenetic classification of fossils reflect the supposed phylogenetic classification?

Research directed toward the solution of the first question is now under way in my laboratory. Support for initial research into the solution of the second question has been granted through an Elizabeth M. Watkins Faculty Summer Fellowship. ~~Funds from this fellowship will be used largely for field work for extensive collecting in Kansas, Missouri, and Oklahoma.~~

The research proposed here will be concentrated on the final two questions although it will also be concerned with the outcome of the first two.

This research is significant to the space program for the following reasons:

1. It will provide important information about the applicability of numerical taxonomy to a continuously evolving lineage of fossil organisms such as might be found on other planets.

2. It will give an estimate of the extent to which phylogenetic conclusions may be drawn from a strictly phenetic classification.

3. It will provide information about the usefulness of numerical taxonomic classification of organisms for stratigraphic and geologic history studies of other planets.

In addition to applications to space science, the proposed research will have the following feedback into basic paleontologic research and the mineral industries:

4. It will provide initial information on similarity among classical and numerical taxonomies of fusulinids.

5. It will lay the groundwork for extensive numerical taxonomic revision of the fusulinids; such work is badly needed to help clarify the over-complicated taxonomy of these important guide fossils.

6. It will, by leading to a revision of the taxonomy of the fusulinids, make them an even more valuable tool to the mineral industries, particularly the petroleum industry, as age and environmental indicator fossils.

D. Relation to present state of knowledge in the field.

With isolated exceptions, numerical taxonomy has not been used by paleontologists, and no extensive study has been made to compare numerical classification of fossils with classical taxonomies. Furthermore, no numerical taxonomic studies have been made of the fusulinids. Numerical taxonomy has been developed primarily at the University of Kansas, but even here it has not previously been applied to invertebrate paleontology.

Two projects now underway in my laboratory are closely related to the proposed research:

1. Numerical cladistics of selected Pennsylvanian and Permian fusulinid species (with R. R. Sokal and J. H. Camin).

This research will reduce an existing phylogenetic tree of 24 fusulinid species to a "most parsimonious" tree, the one with the least amount of parallel evolution. This study will give us an idea of the amount of parallel evolution in the original tree derived by classical methods and provide a firm foundation for evaluating the supposed phylogeny. The same 24 species will be a few of the ones included in

the proposed research. In addition, other species from geologic times not represented in the first study will be used. Research on this project has been completed, and the manuscript is being prepared.

2. Quantitative estimate of variation within a population of fusulinids from the Beil Limestone Member of the Lecompton Formation.

This research will partially answer the question "How much variation do members of a single species of fusulinid show within one locality?"

F. Bibliography of pertinent literature.

1. Anders, E., and Arnold, J. R., 1965, Age of craters on Mars: Science, v. 149, p. 1494-1496.
2. Baldwin, R. B., 1965, Mars: an estimate of the age of its surface: Science, v. 149, p. 1498-1499.
3. Camin, J. H., and Sokal, R. R., 1965, A method for deducing branching sequences in phylogeny: Evolution, v. 19, p. 311-326.
4. Dunbar, C. O., and Henbest, L. G., 1942, Pennsylvanian Fusulinidae of Illinois: Ill. State Geol. Survey, Bull. 67, 218 p.
5. _____, and Skinner, J. W., 1937, The geology of Texas; Part 2, Permian Fusulinidae of Texas: Univ. Texas Bull., 3701, p. 517-825.
6. Leighton, R. B., Murray, B. C., Sharp, R. P., Allen, J. D., and Sloan, R. K., 1965, Mariner IV photography of Mars: Science, v. 149, p. 627-630.
7. Sokal, R. R., 1965, Statistical methods in systematics: Biol. Reviews, v. 40, p. 337-391.
8. _____, and Camin, J. H., 1965, The two taxonomies: areas of agreement and conflict: Systematic Zoology, v. 14, p. 176-195.
9. _____, and Sneath, P. H. A., 1963, Principles of numerical taxonomy: W. H. Freeman, San Francisco, 359 p.
10. Whitting, J., Narin, F., and Stone, C. A., 1965, Mars: age of its craters: Science, v. 149, p. 1496-1498.

G. General plan of work.

1. Select species for study.
    a. Must represent all epochs of Pennsylvanian and Permian time.
    b. Should be species about which phylogenetic speculations have been made in the literature.
2. Obtain and prepare specimens.
    a. Collect specimens in the field.
        1) Grind thin sections.
    b. Borrow specimens from other museums.
        1) Yale's Peabody Museum.
        2) United States National Museum.
        3) Illinois Geological Survey.
        4) University of Illinois.
3. Select and measure or code taxonomic characters.
4. Compute.
    a. Numerical taxonomy phenograms.
        1) Correlation coefficients.
        2) Distance coefficients.
    b. Numerical cladistics cladogram.
    c. Principal components analysis.
5. Draw conclusions.

IV. Facilities.

A. Department of Geology and Museum of Invertebrate Paleontology.

1. Sample washing and preparing area.
2. Thin sectioning equipment.
3. Microscopes and measuring devices.
4. Photomicrographic equipment and darkroom.
5. Laboratory space for research.
6. Drafting space and equipment.
7. Curation and storage for reference materials.

V. Personnel.

A. Principal investigator.

Roger L. Kaesler
Assistant Professor of Geology and Curator, Museum of Invertebrate Paleontology

1. Summer work on proposed research.....100%.
2. Continued during academic year.

B. Faculty associate.

Robert R. Sokal
Professor of Statistical Biology

1. Available for consultation.

C. Other

Research assistant, graduate or undergraduate student for preparing collected materials for study, grinding sections, and making some routine measurements.

1. Summer work on proposed research.....100%
2. Continued during academic year..... 50%

D. Biographic sketch of principal investigator.

I attended the Colorado School of Mines from 1955 until graduation in 1959. I majored in geological engineering with an emphasis on petroleum or "soft rock" geology. At that institution I held a four-year scholarship awarded by the school as well as an Alcoa Foundation scholarship during my senior year.

After graduation I spent one year completing the active duty portion of my military obligation. I entered the University of Kansas in the fall of 1960 with a teaching assistantship. The following year I was awarded the Phillips Petroleum Fellowship. I completed the Master of Science degree in 1962; my thesis was on the taxonomy and distribution of Holocene Ostracoda from the Gulf of California.

I spent part of the summer after completing the master's degree at the Lamont Geological Observatory, Columbia University, with a National Science Foundation Summer Fellowship. I studied deep marine sediment samples and their organic remains and some samples from the Gulf of Corinth, Greece. The results of the study of the Grecian material have not yet been published; the study cannot be completed until more material is collected. (The Royal Hellenic Navy recently offered the services of its Hydrographic Office to collect the necessary samples.)

During the next year and a half I held teaching assistantships and another NSF Summer Fellowship. I continued my studies in geology, particularly in the quantitative and statistical aspects of paleontology.

In February, 1964, I went to the University of Hull, England, to study for seven months with Dr. John W. Neale. Travel and research expenses were financed by a grant-in-aid of research from Sigma Xi; an NSF Summer Fellowship; a fellowship from the British Government; a grant from the Department of Geology, the University of Kansas; and a loan from my bank.

I returned to the University of Kansas in the fall of 1965 and spent that academic year completing my doctoral dissertation with the help of a National Science Foundation Graduate Fellowship. The dissertation developed a quantitative method of evaluating ecologic associations among marine microfossils. It has been accepted for publication with the University of Kansas Paleontological Contributions.

Degrees held: Geol. E., 1959, The Colorado School of Mines
M.S., 1962, The University of Kansas
Ph.D., 1965, The University of Kansas

VI. Budget

A. Salaries	
1. Faculty	
a. Principal investigator *3 months, 100% of time 3/9 of $8200.00	$ 2733.33
b. Faculty associate	0.00
2. Other	
a. Research assistant, graduate or undergraduate	
3 months, 100% of time, 3/9 of $4000	1333.33
9 months, 50% of time	2000.00
B. Permanent equipment	0.00
C. Expendable equipment	
1. microscope slides and coverslips	40.00
2. chemicals	25.00
3. abrasives	20.00
4. photographic film, chemicals, and paper	25.00
D. Travel and field expenses	
1. 10 days field expenses in Kansas @ $12.50	125.00
2. 10 days field expenses out of Kansas @ $20.00	200.00
3. 1000 miles @ $0.09/mile	90.00
E. Publication cost	0.00
F. Computer cost	0.00
Total	$ 6591.66

*Three months' salary rather than the more customary two months' summer salary is requested because this is a pilot study. I hope to accomplish as much as possible during the summer so I will be in a better position to apply for outside research support funds early in the 1966-67 academic year.

To: Committee for NASA Research Proposals

From: Nicholas Willems

Date: January 25, 1966

Title: Analysis of Plates of Variable Thickness

Objectives and Significance:

The objective of this proposal is to further develop the theoretical analysis of plates of varying thickness.

Variations in thickness usually are linear but other types of variations also would be of interest. This proposed initial investigation is concerned with plates of rectangular shape and will consider different types of boundary conditions such as simply supported, clamped and with free edges. The analysis can next be extended to the analysis to continuous plates with different types of intermediate supports such as elastic ribs, simple supports, etc. In addition, plates of skew shape will be investigated showing variations in elastic properties in different directions as occur in anisotropic and orthotropic plates.

This topic is of importance when considering plates of variable thickness as occur in space and aircraft structures. Particularly the analysis of wings and other elements of space structures as orthotropic plates of varying thickness is a logical application of the proposed research.

Results to date

A certain amount of research has been done on the analysis of plates of variable thickness. Fung (5) and Hellan (6) both employed numerical methods to determine deflections of circular plates. Mansfield (1), Suhubi (4) and Centineli (8) solved the problem of rectangular and circular plates for certain kinds of loading with the flexural rigidity being assumed to vary in one direction exponentially as Exp (λx) or Exp (λr). No experimental or analytical work has been done on rectangular or skew plates of linearly variable thickness and different elastic properties in two directions.

Other sources or prospects of future support for this project

Plates of variable thickness are used in aerospace structures.

It is felt that by utilizing the orthotropic plate theory the analysis proposed would be very much applicable to space structures. On the strength of the initial theoretical analysis it is therefore, hoped to obtain support from the aircraft or space industry particularly with respect to the aspect of orthotropic or anisotropic analysis of space structures. It will be advantageous to make an initial study as proposed so as to improve the chances to obtain more research.

Plan of Procedure

(1) To further develop the theoretical analysis of rectangular and skew plates with linearly variable thickness under various boundary conditions and loadings.

To develop a solution technique which is suited for a computer type of operation either by using finite differences or series types of solutions.

Addendum to Proposal for the Study of Solid-State Radiation Detectors

The following description is intended to clarify the nature and function of two items on our recent proposal for the development of solid-state radiation detectors.

Controlled Ambient Apparatus

Solid state radiation detectors are made from high resistivity semiconductor material and therefore are very susceptible to variations in surface conditions and therefore the nature of the ambient in which the devices exist becomes important. The expenditure under this item was intended to explore that ambient dependence.

It was intended to have built a small vacuum manifold (possibly two inches in diameter and 10 inches long) in which could be sealed (through reusable ports in the manifold walls) three or four of the semiconductor devices. The manifold would be connected to a small ion pump (50 1/sec) and a sorption vacuum pump, the two of which would be used to evacute the manifold. Also connected to the manifold would be a valving arrangement whereby various gases (N_2, O_2 water vapor etc.) could be admitted controllably.

It would thus be possible to cycle the devices in various gaseous ambients at various pressures and observe the variation in devices parameters under controlled conditions.

The principal expenditures under this item would be: ion pump and its control unit, the sorption pump and its liquid nitrogen dewar, a thermocouple guage, the components of the manifold, and the valving system.

Oscilloscope

An oscilloscope will be used in many different aspects of this study. For example, it will be necessary to measure the lifetime of minority carriers in the material from which the detectors are to be made. In order to evaluate the electronic apparatus which is to be constructed for this experiment, as well as to actually observe the experimental results and oscilloscope will be required and one with quite high-frequency capabilities. Further, various types of electronic circuitry must be constructed in order to measure the conductivity and the Hall effect in the semiconductor material to be used. In each case an oscilloscope will be needed to evaluate the circuits.

An oscilloscope is a very important piece of test equipment and in order to carry out the work described in this proposal it is virtually essential to have one at hand. There is none presently available in the solid-state laboratory.

F. W. Prosser, Jr. /HET

F. W. Prosser
Associate Professor, Physics

H. E. Talley

H. E. Talley
Associate Professor, Elec. Engr.

FWP:jm
HET:

APPLICATION FOR GENERAL RESEARCH GRANT

NAME Kohlman (Last) David (First) L. (Middle) DATE January 14, 1966

DEPARTMENT Mechanics and Aerospace Engineering ACADEMIC RANK Asst. Prof.

TITLE OF PROJECT Engineering Development of the Parafoil

FIELD OF PROJECT (Please check one)

Arts		Engineering	X	Physical Sciences	
Biological Sciences		Humanities		Social Sciences	

OBJECTIVES AND GENERAL SIGNIFICANCE:

The parafoil is a flexible wing made entirely of nylon and completely self-inflated due to ram air pressure entering the open leading edge. The airfoil shaped cross-section and wing planform gives the device a high lift to drag ratio. It may be packed and deployed like a parachute, but is superior to a parachute because it descends at a much lower glide angle than a maneuverable parachute. Its invention was announced only recently.[1] Although the engineering feasibility of the parafoil has been demonstrated, much analysis, optimization, and development is yet required.

The parafoil has many possible applications. Paramount among these are precision air drop delivery of cargo and personnel; precision soft landing of manned and unmanned space vehicles after re-entry.

The objectives of the proposed research are:

1. Investigate effect of airfoil cross-section and leading edge configuration.
2. Investigate methods of increasing the parafoil aspect ratio (span/width) to improve performance.
3. Investigate improvements to suspension and control techniques.

[1]Nicolaides, John D., "On the Discovery and Research of the Parafoil," Presented at International Congress on Air Technology, Hot Springs, Arkansas, November, 1965.

PLAN OF PROCEDURE

The effect of airfoil cross-section on parafoil performance will be systematically investigated in the K.U. subsonic wind tunnel, using a variety of models constructed of lightweight nylon. An optimum shape and thickness will be sought.

PLAN OF PROCEDURE (cont.)

Attempts will be made to construct flying models with aspect ratios as high as 6.0, using both free flight models and tethered (kite) models. Previous models have had a maximum aspect ratio of 2.0.

The same models will be used to develop less complex suspension and control techniques than presently used.

PLEASE GIVE COMPLETE CITATIONS FOR YOUR THREE MOST RECENT SCHOLARLY PUBLICATIONS:

"Experiments on Sphere Drag, Cylinder Drag, and Stability in Rectilinear Couette Flow," Fluid Mechanics Report 63-1, Massachusetts Institute of Technology, 1963.

"Measurement of Drag of Cylinders and Spheres in a Couette-Flow Channel," The Physics of Fluids, vol. 8, pp. 1013-1017, 1965.

"A Preliminary Theoretical Interpretation of the Effect of Ablation on Dynamic Stability," Sandia Corporation, Report SC-RR-65-483, September 1965.

NUMBER OF YEARS GENERAL RESEARCH FUND HAS SUPPORTED a) THIS PROJECT 0, THIS APPLICANT 0.

RESULTS OF PAST GRANTS IN TERMS OF PROPOSALS, GRANTS, AND CONTRACTS FOR OUTSIDE SUPPORT:

Results not yet announced on NSF proposal previously submitted.

OTHER SOURCES OR PROSPECTS OF FUTURE SUPPORT FOR THIS PROJECT:

There is a definite possibility that NASA will be interested in supporting additional research if the present investigation is successful.

BUDGET:

PERSONNEL (Itemize)

1/4 time graduate assistant	$1,000

SUPPLIES AND EQUIPMENT (Itemize)

Nylon Material	$ 250
Febrication Costs	150
Wind Tunnel Mounting Apparatus	50
Misc.	50
Subtotal:	$1,500

BUDGET: (cont.)

Subtotal:	$1,500

TRAVEL AND OTHER REQUIREMENTS (Itemize)

One trip to consult at University of Notre Dame, Investigator and Graduate Assistant.	$ 200
Total Request:	$1,700

ESTIMATED GE-625 COMPUTER TIME: --- HRS.

A Request

to

The University of Kansas

Committee on Space Science and Technology

for

Funds to Support an Investigation

in

A STUDY OF LITHIUM - DRIFTED SEMICONDUCTOR JUNCTIONS: THEIR DEPENDENCE ON SEMICONDUCTOR MATERIAL PROPERTIES AND THEIR USE AS NUCLEAR PARTICLE DETECTION

Submitted by

F. W. Prosser, Jr.
Physics Department

H. E. Talley
Electrical Engineering Department

Introduction

The development of the lithium-drifted germanium nuclear radiation detector has been very important to nuclear physics research. The use of the lithium-drift technique has permitted the attainment of p-i-n structures in which the depletion layer thickness is in excess of 10mm. Layers of such great thickness are admirably suited to nuclear particle detection, particularly in the area of gamma-ray spectroscopy.

While the feasibility of this type of device has been demonstrated, there are many aspects of it which are not at all well understood. The most eloquent testimony to this is the fact that, while the devices may be obtained commercially, their cost is in the range of $1500-$2000.

A study aimed at understanding and improving the properties of these detectors is clearly in order. Such a study could be of great benefit to both the solid-state device designer and to the nuclear physicist. The former would advance the knowledge of solid-state materials, the latter would obtain a radiation detector far superior to any previously available.

An investigation of the type proposed here is expected to lead substantially beyond a study of radiation detectors. The lithium-drift devices depend upon physical principles which have been inadequately explored. Part of these will be analyzed in developing good radiation detectors, but others can only be studied by way of longer range projects. This applies, in particular to the interaction of crystalline imperfections and lithium diffusion and drift. Assuming that the initial program is successful, it is expected that such investigations will occupy research efforts for several years and sponsorship will be sought for these.

The project outlined in this proposal is that of studying lithium p-i-n devices. The first section of the proposal will discuss the importance of such devices in nuclear physics research, the second section will outline the nature of the program from the solid-state device point of view.

Lithium-Drift Devices in Nuclear Physics Research

In spite of the infancy in the development and understanding of this type p-i-n junction, its use in nuclear spectroscopy has already made possible a significant improvement in several research areas and promises much more. Much of the research in the Nuclear Structure Laboratory requires the detection of gamma radiation with devices whose output is proportional to the energy of the detected photons. Also, in many cases, the strength of the source of radiation is unavoidably weak, so that a useful detector must have a high probability of detecting any gamma ray striking it. The replacement of gas proportional detectors by scintillation detectors, beginning around 1950, with the consequent increase in efficiency of a factor of 100 or more, caused a major revolution in the quality of nuclear physics research and in the complexity of problems which could be meaningfully investigated. However, the scintillation detector, as was the proportional counter, is capable of only moderate energy resolution, in the order of a few percent, and high resolution measurement of gamma radiation has continued to require the use of the extremely inefficient process of magnetic analysis of energetic electrons produced by gamma radiation incident on thin films.

The advent of the germanium p-i-n junction detector, with a resolution comparable to all but the ultimate in magnetic charged particle analysis, promises another, equivalent change in the very concepts of nuclear spectroscopic experimentation. The present limitations are the low efficiency, associated primarily with the small size of presently available detectors, and their high cost when obtained commercially, associated with the uncertainties arising from the current lack of understanding of the very nature of the physical principles of this type detector and the consequent uncertainties in their production.

We, of the Nuclear Structure Laboratory, are therefore eager to participate in this attempt to find and better understand the critical factors in this solid state phenomenon and to help with the testing, as well as to employ the successful samples in our nuclear physics research.

Solid-State Device Studies

While solid-state radiation detectors are available on a limited commercial basis, there are many aspects of them which are not all well understood. There are a number of compelling reasons for trying to develop a thorough understanding of the essential aspects of their performance. Chief among these reasons are three:

a. The correlation of semiconductor materials properties with device performance is very poor.
b. Substantial improvement in device performance may be expected from the application of carefully analyzed fabrication techniques, particularly in the area of device efficiency.
c. There is need to extend the capabilities of the devices (particularly toward achieving larger active areas) and to attempt to lower the unit cost from the present range of $1500-$2000.

The program to achieve the goals implicit in the items listed above may be divided into two more or less parallel activities. First, silicon and germanium radiation detectors will be built by adapting those techniques which have proved to be essential in developing high-performance, high-reliability and low-cost transistors and diodes. Second, as the characteristics of the fabricated devices are analyzed, studies will be made of the properties of the semiconductor material from which they were made. Among these studies will be low temperature Hall effect measurements, the use of both x-ray and chemical etching techniques to investigate the nature of the imperfections in the semiconductor material, and analysis of the behavior of the minority carrier lifetime.

It is essential that these detailed materials studies be made, since there is no adequate understanding of what semiconductor material parameters are essential. For example, there appears to be the common feeling that certain germanium ingots will yield good detectors while other "identical" ingots will yield no good units. At present the resolution to this difficulty appears to lie in the brute force technique of throwing away the bad ingot and looking, in a purely random fashion, for a good one. It is not surprising under these circumstances that the device cost is high, and that there are many avenues available to improve the device performance.

In order to explore some of these avenues we are requesting that $14,650 be made available to finance project expenses. Listed in the appendix to this proposal are the items for which this money would be spent. Most of these are self-explanatory. To be included under the section marked Salary is that for one graduate assistant for nine months and half-time salary for one of us (H. E. Talley) for two months during the summer of 1966. The money shown under Travel would allow the two authors of this report to visit organizations who have made and used semiconductor detectors. In this way we would hope to be able to avoid having to repeat much of the work which they have done.

The program discussed in this proposal is expected to be of substantial value to both the Physics Department and the Electrical Department. Working together we would hope to advance the understanding of the nature of solid-state radiation and semiconductor materials while, at the same time, making these detectors available to the Nuclear Structure Laboratory for evaluation and for nuclear physics research.

One further point should be made. The investigation which would be initiated by way of this proposal will have consequences far beyond simply producing a detector of nuclear radiation. The nature of the interaction of the lithium with crystalline properties of the semiconductor and the possibility of studying other impurities which should behave in a fashion similar to lithium all promise to yield valuable knowledge in the field of solid-state materials. It is expected that the program started here would be continued for several years, and that sponsorship by other agencies would be obtained to support this research.

F. W. Prosser, Jr.

H. E. Talley

Proposed Budget

Hall effect magnet and control circuits		$ 1900
Laminar flow clean enclosure		1500
Semiconductor material		1000
Dewar (Liquid nitrogen storage)		300
Dewar (Device evaluation)		300
Oscilloscope		1500
Semiconductor polishing apparatus		750
Chemicals and Supplies		400
Controlled ambient apparatus		2500
Salaries		3900
Travel		600
	Total	$14,650

THE UNIVERSITY OF KANSAS
Lawrence, Kansas

Department of Zoology Snow Hall

Subject: A proposal to study the thermal denaturation profiles of DNA from a variety of animals.

To: Dean William Smith, Chairman, NASA Research Grants Committee, University of Kansas

From: Dr. Charles A. Leone, Department of Zoology
and
Dr. William D. Baxter, Department of Zoology

I. INTRODUCTION

The identification and mensuration of extraterrestrial life is of importance to the Life Sciences aspects of the NASA research program. Studying the molecular composition of unusual organisms and especially those not ordinarily encountered in biochemical studies gives us experience in dealing with the kinds of problems that will arise when the exotic, extraterrestrial life forms become available. The biological data gained is a worthy justification of the work in its own right. The molecule of choice in this proposal is deoxyribonucleic acid (DNA), of importance in determining the hereditary structure of organisms. DNA is often considered to be a major component of primeval living systems as we know them.

II. PROPOSAL

Marmur and Doty (1) have shown that the nucleotide base composition of deoxyribonucleic acid (DNA) is related to its thermal denaturation temperature. When native DNA is heated in dilute salt solution a marked increase in the extinction coefficient occurs when the temperature reaches the point at which the double stranded molecules are altered to the single stranded state. The temperature corresponding to the midpoint (T_m) of this transition is linearly related to the average DNA base composition; a higher guanine-cytosine content confers a higher thermal stability. Moreover, Marmur and Doty (2) have demonstrated that the relationship between T_m and base composition is a linear one and the actual percent guanine + cytosine can be calculated if the thermal denaturation profile for the DNA is known.

One would expect orderly change in DNA base-ratios during evolution. This expectation has led to attempts by the above investigators and others to use T_m determinations as a means of ascertaining taxonomic and/or phylogenic relationships between organisms. In virtually every case, however, this technique has been applied to the nucleic acids from microorganisms with results that are consistent with suspected relationships or unique environmental growth conditions.

To our knowledge these procedures have not been extensively applied to the analysis of DNA from invertebrates, probably owing to problems related to the collecting of the animals and the extraction of nucleic acid from

them. We have made attempts in our laboratory to detect significant differences between the T_m's of DNA from a variety of vertebrates and while we can show these differences between members of different classes (reptile vs. mammal, for instance) it has not been possible, even with the sensitive equipment at our disposal, to detect statistically significant differences between DNA's from animals in the same class. It is, therefore, our intention to apply this technique to the analysis of nucleic acids obtained from a wide variety of organisms, both vertebrate and invertebrate, in an attempt to clarify the phylogeny of these animals at the class or family level.

A short discussion of the interpretation of results obtained from studies of this sort is in order. It is readily apparent that, during evolutionary modification of the genetic material of a number of animals, changes could occur in nucleotide base sequence that would not alter the over all guanine + cytosine content of the DNA. Alternatively, it is possible that two animals originally possessing quite different DNA compositions could, by convergence, evolve nucleic acid base ratios that are very similar even though they are morphologically dissimilar. The two situations above would lead to cases where the T_m of the DNA from these animals would be similar and little could be said as to these animals' phylogeny. However, it is also possible that, owing to environmental factors, two groups of primitively unrelated animals could evolve quite similar morphological characteristics through changes of a few genes while the major portion of their genetic material remains relatively unaltered. These organisms, on the basis of morphological taxonomy, would be erroneously judged as closely related and belonging to a common phylogenetic line. The demonstration that these organisms differ greatly in the T_m's of their DNA would indicate that a high degree of morphological convergence had occurred. If, as some modern authors suggest, several major invertebrate groups are not true phylogenetic groupings, but rather, are assemblages of animals at similar grades or levels of morphological organization, it would be essential to have measures of genetic relatedness among the members of these groups. If the groupings are phylogenetic, measures of the genetic relatedness among them are essential to an understanding of biochemical evolution.

Materials and Methods

Obtaining of animals for DNA extractions. Since our desire is to compare DNA from diverse animal groups, it will be necessary to collect invertebrates locally, and to have shipped to our laboratory, from a marine animal supplier, live representatives of several invertebrate classes. We have adequate aquarium facilities for keeping them alive and healthy until time of sacrifice.

Isolation of DNA. We have had extensive experience in isolating and characterizing the DNA from a wide variety of vertebrates. The procedure used is a slight modification of the method of Marmur (3) and it is believed that this general method can be adapted for the isolation of DNA from the tissues of invertebrates. A major portion of the early work in this study

would center on determining optimal isolation procedures.

Characterization of DNA samples. The DNA extracted would be assayed for a) their concentration and purity, b) the extent of denaturation, and c) their thermal denaturation profiles.

a) Concentration and purity - Concentration will first be determined by phosphorous analysis (4), and the extinction coefficient at 258 mμ determined. Later quantitation will be by spectroscopy. The purity of samples will be checked by the biuret reaction and ultra-violet spectrum analysis to guarantee that the DNA is protein free. b) Test for DNA denaturation - The molecular state of the sample will be assayed by the Shack test (5) which allows an estimation of the extent of denaturation of the native DNA during extraction and storage. A maximum permissible amount of denaturation will be established and samples not compared which exceed this limit. c) Determination of thermal denaturation profiles - We have, during the past year, constructed an automatic recording thermospectrophotometer for use in determining thermal denaturation profiles. The basic units in this set-up are a B&L Spectronic 505 spectrophotometer, modified for time-rate read-out into one channel of a dual-channel strip-chart recorder; water-jacketed cuvette holders which allow the temperature of the DNA solution in the reference cuvette to be held at a reference value and the temperature of the solution in the sample cuvette to be slowly elevated; and finally, a telethermometer assembly with a probe in the sample cuvette, which allows recording solution temperature on the other channel of the recorder. As can be seen, this system allows the simultaneous recording of changes in optical density and temperature. The T_m for the sample can then be calculated from the single strip.

We have found the system described above to give highly reproducible results between determinations of DNA from the same source. It appears that this system will allow us to detect statistically significant differences in T_m as small as 0.4°C. From Marmur and Doty's calculations (2) this would be a difference of approximately 1 mole percent guanine + cytosine. It is believed that the detection of this amount of difference is sufficient to make T_m determinations of great value in phylogenetic studies.

References

1. Marmur, J. and P. Doty (1959) Nature, 183, 1427.
2. Marmur, J. and P. Doty (1962) J. Mol. Biol. 5, 109.
3. Marmur, J. (1961) J. Mol. Biol. 3, 208.
4. Allen, R. J. L. (1940) Biochem. J. 34, 858.
5. Shack, J. (1958) J. Biol. Chem. 233, 667.

III. FACILITIES, SERVICES, and OPERATIONAL PLAN

The work in this proposal will be done in Dr. Leone's laboratory which is well-equipped for this purpose. Dr. William Baxter, of this department, will serve as Research Associate on the project. He will be responsible for implementing and executing the laboratory work. Assisting Dr. Baxter will be Mr. Fred C. Brown, NSF undergraduate research fellow. Normal laboratory support such as electronic servicing of our instruments, some animal care, glassware washing, etc. will be provided from other sources available to Dr. Leone.

IV. PERIOD OF RESEARCH. 1 June 1966 - 31 August 1966

V. BUDGET

1.	Salary for Dr. William Baxter, 2 mos. Full time @ 722.00/mo.	$1,444.00
2.	Supplies	
	a. Animals	300.00
	b. Chemicals, sea water, etc.	250.00
	Total	$1,994.00

APPLICATION FOR NASA RESEARCH GRANT

Description of Research Project

In the microbial world there exist a variety of organisms which thrive under conditions which are considered extreme for other forms of life Thus some organisms live only in solutions which have a high salt concentration (Halophiles), some only at cold temperatures (Psycrophiles) and some only at high temperatures (Thermophiles). We have recently undertaken a study to determine the reasons for thermophilicity. We are concentrating at the present on the obligate anaerobic thermophile Clostridium thermosaccharolyticum, an organism which was first found in spoiled canned goods.

In the limited number of cases studied it has been found that enzymes extracted from thermophilic organisms in general show a greater heat stability than those from organisms which grow at "normal" temperatures (25-37°C). Our immediate aim is to determine the reasons for this greater heat stability. Our future aims are to study the complete biochemistry of a thermophile. This will include analysis of the nucleic acids, ribosomes and protein synthesizing systems.

The initial approach has been to learn something about the metabolism of the organism. It uses glucose as a carbon source but the pathway of glucose metabolism is not known. By working with resting cells, we have found that butyric acid, acetic acid, CO_2 and H_2 are products of the fermentation. We are currently doing quantitative experiments to determine the stoichiometry of the fermentation. The knowledge of how glucose is

metabolized will give us an indication of what enzymes are likely to be present in the cell in relatively high concentrations. The next step will be to isolate and purify a few of these enzymes and study their chemical and physical characteristics in order to compare them with similar enzymes from other organisms. These studies would include amino acid, ultracentrifugal, electrophoretic, diffusion and viscosity analyses in order to determine the size and shape of the proteins.

We have been working on this problem for approximately one year. In addition to the headway made in the study of the pathway of glucose fermentation mentioned above, we have been engaged in purifying the protein, ferredoxin from this organism. Chemical and physical studies of this protein will soon commence.

It is, of course, quite conceivable that the forms of life which may be encountered in the exploration of space may exist under conditions which we consider extreme. We are in a position to learn something about the biochemistry of such forms of life by studying those which live on this planet.

Period of Time Support is Requested: July 1, 1966 - June 30, 1967

Budget

Research assistant	- 1/2 time - 12 months	$3,100
Glassware and chemicals		900
Total budget		$4,000

Richard H. Himes
Assistant Professor

Research Proposal
to
K. U. NASA Committee

It is desired to investigate the free vibrational frequencies and corresponding mode shapes of an axisymmetric, homogenous, isotropic hollow torus. Very little research has been conducted on the vibrations of this type of shell. One notable paper in this area is "Free Vibrations of the Prestressed Toroidal Membrane," by A. A. Liepins, Report No.474, NASA Contracts NASw-600 and NASw-881, in which shell equations of motion were utilized to obtain the solution. Naturally, in the shell approach there was no dependence of the displacements upon the radial coordinate.

In the proposed study the basic displacement equations of elasticity will be nondimensionally written for the torus; zero normal and tangential stress boundary conditions will be written in terms of nondimensional displacements to complete the formulation of the problem.

The above two elasticity equations of motion, resulting from summing forces in the radial and tangential directions in any cross-section, are linear; however, they contain complicated coefficients which are functions of the polar coordinates of the section, r and θ. Hence, these differential equations will be replaced by a pair of finite difference equations in the unknown displacements u_r and u_θ, each of which is of course a function of r and θ.

Half of the cross-section (using symmetry) will then be divided into a net by semi-circles concentric with the boundaries and by rays extending from the center of the cross-section.

A program will then be written which will write the difference equations, i.e., calculate the non-zero coefficients of the two difference equations, each of which is written at every mesh point in the annular region. Such a program will yield all equations for a given torus once six items are specified-Poisson's ratio, the inner radius, the radial and tangential mesh increments, the number of interior circles of subdivision of the section, and the ratio of the two torus radii.

When writing the difference equations on the inner and outer boundaries, undesirable unknown values of u_r and u_θ will be encountered at points exterior to the annular region. These unknowns will be expressed in terms of desirable unknowns (u_r's and u_θ's within the region) by means of the boundary conditions.

The study will then become an eigenvalue problem, for in the matrix of coefficients of the generated equations there will be an unknown frequency parameter subtracted from each element of the principal diagonal. The set of homogeneous equations will have a solution if and only if the determinant of the coefficients vanishes; this will yield the lower frequencies. Then the mode shapes are easily calculated.

After some experimental verification, the proposed study should yield the following results:

(1) Determination of frequencies and mode shapes for any open torus;
(2) Decreasing the thickness should check the toroidal membrane results; decreasing both the thickness and torus radii ratio should check membrane results for cylindrical shells;
(3) The effects of thickness, torus radii ratio, and Poisson's ratio upon frequencies and mode shapes will be determined;
(4) It is believed that this problem will mark the first attempt at solving partial differential equations in more than one independent variable by means of differences. Therefore, of mathematical interest will be the effect of finer and finer nets upon the convergence of the solution to such a problem.

The previous statements on the proposed project have been given to Prof. B. Barr since it is my opinion that this should merit a separate research project. In the meantime, David McGill is proceeding with the work which is to be his Ph.D. dissertation. Mr. McGill will need support during the second semester.

One of the main needs besides support of McGill is a larger digital computer. Since the 625 will not be installed prior to March, 1966, we would like to utilize the IBM 7094 at the Kerr-McGee Company. To do this we will need the necessary travel funds and expenses associated with the use.

I recommend that sufficient funds be allocated from the K. U. NASA Research Funds to continue this project. If the project is accepted by the NASA Committee, the funds will, of course, be refunded.

The funds needed are:

Salary for David McGill, 1/2 time	second semester	$1300
	summer	600
Travel and miscellaneous expenses		600
	Total	$2500

Kenneth H. Lenzen, Professor

Application for support from the University NASA Program Grant for:

NATURAL ENVIRONMENTAL FACTORS IN BEHAVIOR OF THE OPOSSUM, RACCOON, AND STRIPED SKUNK

June 1, 1966 to May 31, 1967

$1,425.30

Hampton W. Shirer

Department of Comparative Biochemistry and Physiology
Department of Electrical Engineering

and

Henry S. Fitch

Department of Zoology

In following the day to day home range activity of a number of opossums, raccoons, and striped skunks by radio location on the University of Kansas Natural History Reservation since late summer of 1965, we have found considerable variation in the extent of the daily range from individual to individual and in a given individual from one time to another. In particular, it has been noted that on occasions when the weather was quite cold some individuals remained in their den for prolonged periods ranging up to a few weeks, while others remained sheltered for only the period during the most severe cold. With respect to the general question on mechanisms of organism adaptation to charactertistics of its environment, this comparative study of the home range activity of these phylogenetically distinct mammals is to continue over one or more full seasons. This proposal seeks support for study of the relationship of natural environmental factors to specific behavioral patterns as a function of species, age and sex and to relate physiological reactions to behavior and environmental conditions.

Animals sampling species, age and sex equipped with radio transmitter collars will continue to be followed daily in their home range activity by tracking with portable direction finding receivers. To record period and frequency of specific den occupancy, transponders will be used to retransmit the animal's signal to the Central Recording Facility. Environmental conditions will be monitored by a standard climatological station installed in the headquarters valley, supplemented by several temperature sensors located in ecologically unique sites.

Surgically implanted, short range transmitters will be used to telemeter body temperature and heart rate to the Central Recording Facility via the den transponders. Multiple channel central analog recording equipment is to be replaced with computer compatible, digital system.

Correlation of home range behavior with details of environmental conditions will provide information as to what factors initiate particular response patterns. Of particular interest is comparing the relative roles of behavior (shelter seeking) and metabolic changes in energy conservation. Body temperature and heart rate will suggest metabolic adjustments made by animals during stays of different periods within dens of varying thermal characteristics.

Funds are requested for the full time summer salary (2 months) of a graduate research assistant, Mr. David Pippitt. In addition, consummable supplies in the form of electronic components for telemeter transmitters, transponders, and minor receiver modifications; chemicals; drugs; and graphic materials are required.

Funds from other sources (National Science Foundation) are available for Central Recording Facility modifications and environmental sensing.

Graduate research assistant, full time ($444.00).

2 months		$888.00
FICA at 4.2%		37.30
Scientific supplies		500.00
	Total	$1425.30